DEHYDRATION STUDIES OF 8a-METHYLDECAHYDRONAPHTHALEN-4a-OLS

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by

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ABSTRACT

A series of 8a-methyldecahydronaphthalen-4a-ols labelled at C(1) with deuterium have been prepared and their reactions in H_2SO_4-Ac_2O-AcOH and $SOCl_2$-pyridine studied.

The dehydration of 8a-methyl-*cis*-decahydronaphthalen-r-4a-ol-t-5-*d* (27b) and 8a-methyl-*trans*-decahydronaphthalen-r-4a-ol-t-5-*d* (28b) in H_2SO_4-Ac_2O-AcOH occurs with no loss of deuterium. In each case a proton *syn* to the departing C(9)- moiety is lost. No products of skeletal rearrangement or methyl migration were detected. In the dehydration of 8a-methyl-*trans*-decahydronaphthalen-r-4a-ol-c-5-*d* (28g) in H_2SO_4-Ac_2O-AcOH significant loss of the C(1) deuterium occurs. Reaction of 5*α*-cholestan-5-ol-4α-*d* (3f) with H_2SO_4-Ac_2O-AcOH gives a mixture (1:1) of cholest-4-ene (14a) and cholest-5-ene-4α-*d* (7d). The results of these studies have been rationalized in terms of the intermediacy of a tight ion pair in which the departing oxy-anion acts as base in the abstraction of an adjacent proton.

The results of dehydration of 8a-methyl-*cis*-decahydronaphthalen-r-4a-ol-t-5-*d* (27b) and 8a-methyl-*trans*-decahydronaphthalen-r-4a-ol-t-5-*d* (28b) in $SOCl_2$-pyridine contrast with those obtained for H_2SO_4-A_2O-AcOH. Dehydration occurs with 43 and 35% deuterium loss respectively, and the reactions are thought to occur *via* an E2 type process. Reaction of

t-8a-hydroxy-4a-methyl-*trans*-decahydronaphth-r-1-yl acetate (28h) with $SOCl_2$-pyridine gave c-4a-methyl-1,2,3,4,4a,5,6,7-octahydronaphth-r-1-yl acetate (23f). Reaction of t-8a-hydroxy-4a-methyl-*trans*-decahydronaphth-r-1-yl acetate (28h) in H_2SO_4-Ac_2O-AcOH gave c-8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphth-r-1-yl acetate (24b,50%), c-8a-methyl-1,2,3,5,6,7,8,8a-octahydronaphth-r-1-yl acetate (50a,33%), 4a-methyl-2,3,4,4a,5,6,7,8-octahydronaphth-1-yl acetate (23e, 8%), and 4a-methyl-*trans*-decahydronaphthalen-1-one (32a,8%).

The rearrangement of 4a,5-epoxy-c-8a-methyl-*trans*-decahydronaphth-r-1-yl acetate (25b) with BF_3-etherate in benzene gave c-8a-methyl-1,2,3,7,8,8a-hexahydronaphth-r-1-yl acetate (62a,30%), c-8a-methyl-5-oxo-*trans*-decahydronaphth-r-1-yl acetate (32b,26%), 4a-fluoro-c-5-hydroxy-8a-methyl-*trans*-decahydronaphth-r-1-yl acetate (60c,40%) and an unidentified aldehyde (4%). Rearrangement of 4a,5-epoxy-c-8a-methyl-*trans*-decahydronaphth-r-1-yl acetate (26c) with BF_3-etherate in benzene gave c-8a-methyl-1,2,3,7,8,8a-hexahydronaphth-r-1-yl acetate (62a,34%), the aldehyde (65,6%), c-8a-methyl-5-oxo-*cis*-decahydronaphth-r-1-yl acetate (31b,7%), c-8a-methyl-5-oxo-*trans*-decahydronaphth-r-1-yl acetate (32b,4%), 4a-fluoro-t-5-hydroxy-c-8a-methyl-*cis*-decahydronaphth-r-1-yl acetate (61b,22%) and two unidentified compounds (27%).

Thermodynamic parameters for the equilibration of the conformational enantiomorphs (37) and (38) of

8a-methyl-*cis*-decahydronaphthalen-4a-ol have been determined as E_a = 69.8 ± 0.9 $kJmol^{-1}$, $\Delta H^{\ddagger}$ = 66.7±1.3 $kJmol^{-1}$ and $\Delta S^{\ddagger}$ = + 12 ± 5 $JK^{-1}mol^{-1}$. It has been shown that conformer (39) of 4a-methyl-*cis*-decahydronaphthalen-1-one is 1.25 $kJ^{-1}mol^{-1}$ more stable at 200K than conformer (40), and the thermodynamic parameters for the conformational interconversion of (39) → (40) have been determined as E_a = 42.9 ± 0.7 $kJmol^{-1}$, $\Delta H^{\ddagger}$ = 41.0 ± 0.7 $kJmol^{-1}$, and $\Delta S^{\ddagger}$ = -20 ± 3 $JK^{-1}mol^{-1}$.

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INTRODUCTION

This thesis is primarily concerned with dehydration studies of 8a-methyldecahydronaphthalen-4a-ols. Analogous reactions of C(5)-hydroxy steroids have received considerable attention. The decahydronaphthalene system however does not have the complexities of steroid rings C and D and is therefore an excellent model substrate.

Dehydration of C(5)α-hydroxy steroids in acetic acid-acetic anhydride with catalytic quantities of sulphuric acid have been of interest since Westphalen[1] noted that 3β,6β-diacetoxy-5α-cholestan-5-ol (1a) rearranged under these conditions to give 3β,6β-diacetoxy-5-methyl-19-nor-5β-cholest-9-ene (2) (fig. 1)[2-6]. Sulphuric acid or potassium hydrogen sulphate act as catalysts for the dehydration, while other acids promote acetylation of the hydroxyl function[7-9]. Dehydration in the presence of H_2SO_4 is thought to occur *via* the intermediacy of a rapidly formed acetyl sulphonate ester (fig. 1). The reaction is first order in alcohol, acetic anhydride and sulphuric acid. A reaction constant ρ* of -4.8, which was determined from kinetic measurements on a series of C(6)β- substituted 3β-acetoxy-5α-cholestan-5-ols, indicates the development of an electron deficient centre in the rate determining step.[8] The orientation of the C(5)-leaving group and C(4) and C(6) substituents have a profound effect on the course of the reaction. In the H_2SO_4-Ac_2O-AcOH promoted dehydrations of 4-acetoxy-5α-cholestan-5-ols

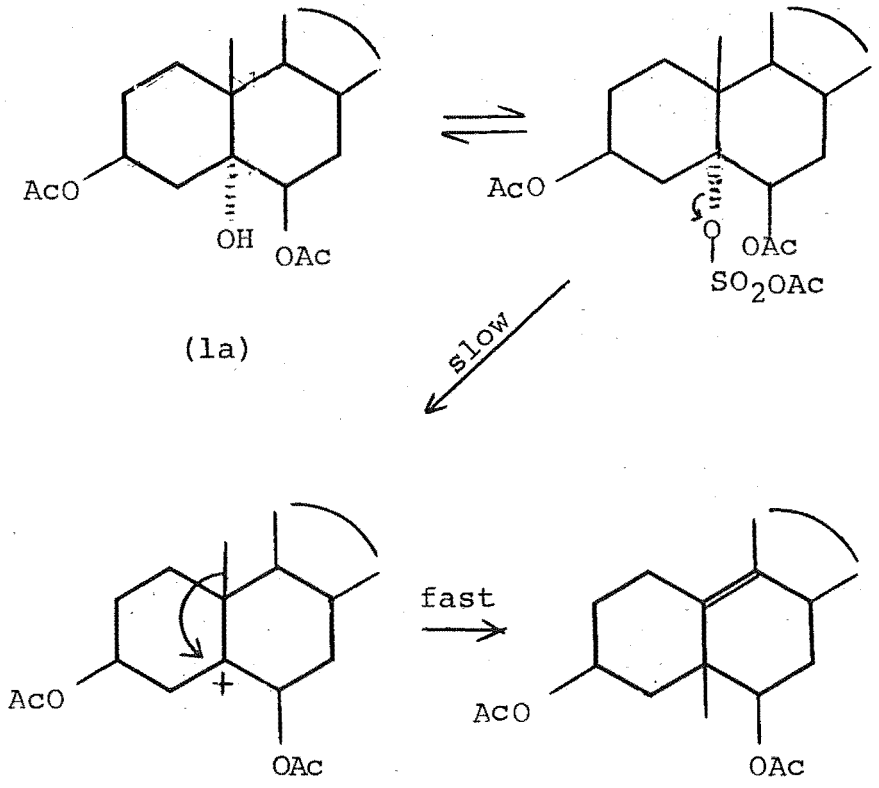


Figure 1: The Westphalen Rearrangement.

the 4β-acetoxy isomer (3a) rearranges to give a 20:4.5:1 mixture of the $\Delta^{9,10}$-, $\Delta^{8,14}$-, and $\Delta^{13,17}$- olefins (4,5 and 6a) respectively, in 77% yield. In marked contrast the C(4)α isomer (3b) gives a mixture of cholest-5-en-4α- and 4β- yl acetate (7a and 7b). Similar dehydration of 4β-acetoxy-5β-cholestan-5-ol (3c) gives a mixture of 4β,5-diacetoxy-5β-cholestane (3d), cholest-5-en-4α-yl acetate (7a and 7b), and 5α-cholestan-4-one[11] (8). The ketone formed from 4β-acetoxy-5β-cholestan-5-ol (3c) is

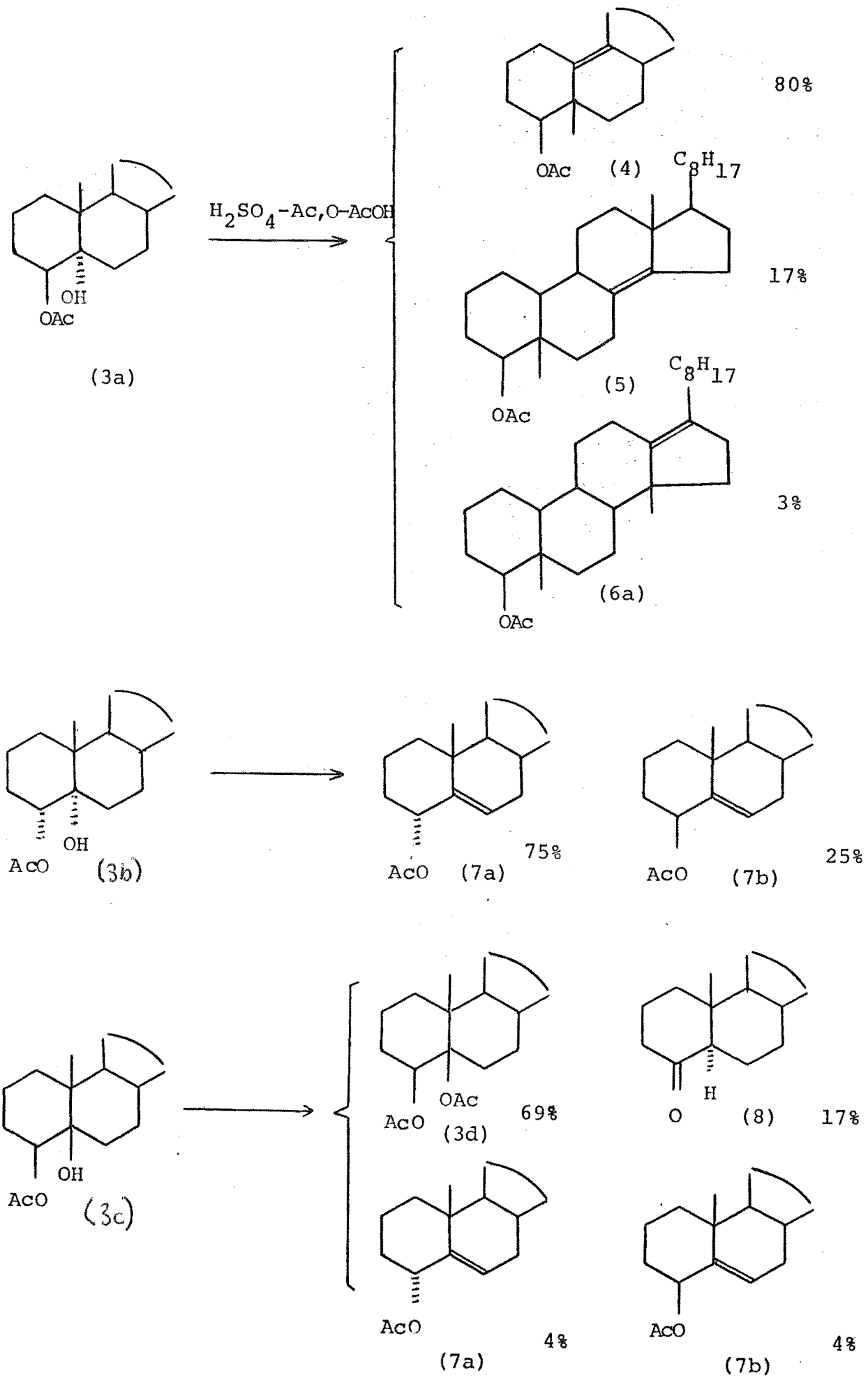
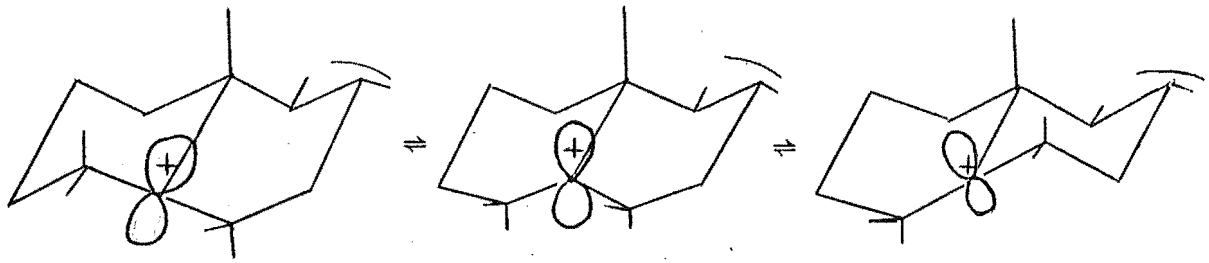

H2SO4-Ac,O-AcOH
OH
OAc
(3a)
OAc
(4)
80%
C8H17
OAc
(5)
17%
C8H17
OAc
(6a)
3%
OH
AcO
(3b)
AcO
(7a)
75%
AcO
(7b)
25%
OH
AcO
(3c)
OAc
AcO
(3d)
69%
H
O
(8)
17%
AcO
(7a)
4%
AcO
(7b)
4%

Figure 2.

thought to arise by elimination of the C(4)α-hydrogen to give the enol acetate (9) which on 'workup' undergoes hydrolysis[11,12] (fig. 2).

These results have been rationalized in terms of the relative stabilities of the various conformations of the C(5)-carbonium ion. It is believed that processes subsequent to carbonium ion formation are competitive with equilibration of the different conformations of the carbonium ion. The conformation of the initially formed carbonium ion is thought to be important in determining product distribution.[11] The strain introduced into rings A and B of the steroid nucleus as the hybridization at C(5) changes from sp^3 to sp^2, may be accommodated by conformational adjustment in ring A, or ring B, or by adjustment in both rings A and B (fig. 3).



10 ⇌ 11 ⇌ 12

Figure 3.

In conformations (10) and (12) (fig 3) the axial C-H bonds on C(4) and C(6) are aligned with the p- orbital at C(5) and therefore 1,2- elimination is favoured over C(10)- methyl migration. In conformation (11) however the C(10)-methyl bond is suitably positioned for migration to occur.

In the reaction of 4β-acetoxy-5α-cholestan-5-ol (3a), the presence of a 1,3-diaxial acetate - methyl interaction introduces steric strain to conformation (10). This interaction is relieved in conformation (12). However the development of the ion in this conformation could only occur at the expense of a clash between the C(5)α- leaving group and the C(7)α-H and the C(9)α-H. The high yield of products resulting from C(10)-methyl migration in this reaction suggests that conformation (11) of the carbonium ion is important (fig 3). The abscence of products of methyl migration in the dehydration of 4α-acetoxy-5α-cholestan-5-ol (3b) precludes the intermediacy of the carbonium ion in conformation (11) in this reaction. While 4β-acetoxy-5β-cholestan-5-ol (3c) would, superficially at least give the same ion as from 4β-acetoxy-5α-cholestan-5-ol (3a) the reaction products are different.

Some authors[13-16] maintain that in the Westphalen and related rearrangements C(10)- methyl migration may be concerted with C(5)-O bond cleavage. As evidence they cite both the abscence of products of methyl migration from 5β-hydroxy steroids and the rate enhancement observed

in the dehydration of C(10)β-ethyl steroids.[16] The observed rate change can however be accounted for by the steric change and inductive effects of replacing the methyl by an ethyl group. The absence of products of methyl migration from C(5)β-hydroxy steroids does not however preclude the intermediacy of C(5)-carbonium ions in the dehydration reactions of these alcohols.

Dehydration of 3β,6β-diacetoxy-5α,9β-cholestan-5-ol (13) under Westphalen conditions gives two spiran olefins (14) and (15)[17,18]. These result from migration of the C(1)-C(10) bond on the α-face of the molecule (fig 4). The configuration at C(5) is therefore retained and Coxon, Harishorn and Muir[17,18] cite this as evidence that Westphalen rearrangements occur *via* discrete carbonium ion intermediates.

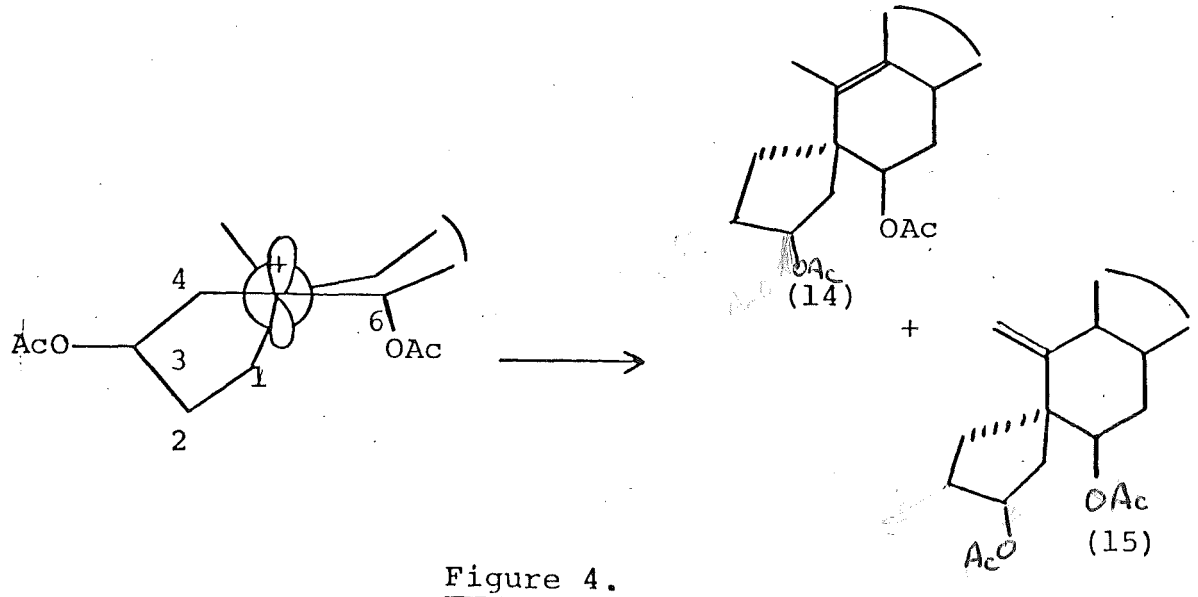


Figure 4.

Whereas the products arising from methyl migration under Westphalen conditions have been thoroughly investigated the alternative and competing pathways involving 1,2-

elimination to produce Δ^4- and Δ^5- olefins have received relatively little attention. In some cases 1,2-elimination is the major reaction pathway. 5α-Cholestan-5-ol (3e) under Westphalen conditions gave a (ca. 7:3) mixture of cholest-4-ene (14a) and cholest-5-ene (7c). Small quantities of 5β ,14β-dimethyl-18,19-bisnorcholest-13(17)-ene (6b) were indicated by high pressure liquid chromatography.[19]

Dehydration of steroidal C(5)-alcohols with thionyl chloride-pyridine is thought to proceed *via* a chloro-ester intermediate.[20] Dehydration of 5α-cholestan-5-ol (3e) under these conditions gave a 1:1 mixture of cholest-4-ene (14a) and cholest-5-ene (7c)[21]. For unsymmetrical alcohols where a choice of reaction paths is possible elimination has been found to occur to the more substituted carbon. For example reaction of 6α-methyl-5α-cholestan-6β,3β-diol (15) with thionyl chloride-pyridine gave the more hightly substituted Δ^5-olefin (16a). In contrast dehydration of 3β-acetoxy-6β-methyl-5α-cholestan-5-ol (1b) gave 3β-acetoxy-6β-methylcholest-4-ene (17), a product of *anti*- elimination, rather than 3β-acetoxy-6-methyl-cholest-5-ene[22] (16b) (fig. 5). In a comprehensive study Shoppee *et al.*[23,24] observed a preference for elimination to occur away from a C(4) or C(6) acetoxy substituent in the thionyl chloride - pyridine induced eliminations of C(5)- hydroxy steroids. For example 4α- and 4β-acetoxy-5α-cholestan-5-ols (3b) and (3a) on reaction with $SOCl_2$-pyridine gave 4α- and 4β-acetoxycholest-5-ene (7a) and (7b) respectively. Similar dehydration of 6α-

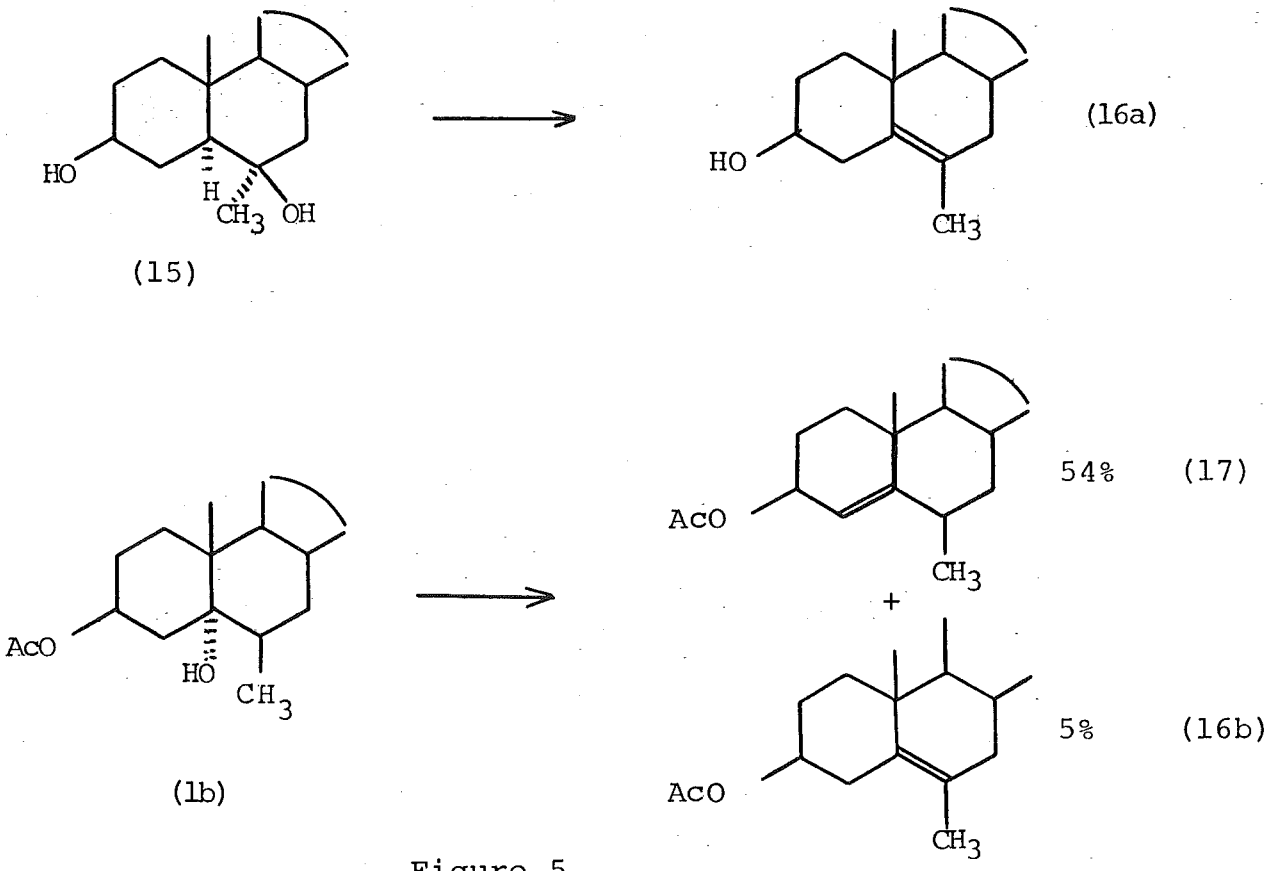


Figure 5.

and 6β-acetoxy-5α-cholestan-5-ol (18a) and (18b) afforded 6α- and 6β- acetoxycholest-4-ene (14b) and (14c) respectively. The stereochemistry of the proton lost in the elimination of water from 4α-acetoxy-5α-cholestan-5-ol (3b) in $SOCl_2$-pyridine was determined by Bathurst *et al.*[11] The C(6)β-position was labelled with deuterium and deuterium was substantially lost in the reaction (fig. 6).

For elimination from 3-methyl-3-hydroxy-steroids and 4-methyl-tertiarybutylcyclohexan-4-ols with $SOCl_2$-pyridine a marked preference for formation of exocyclic olefin was observed. This preference for

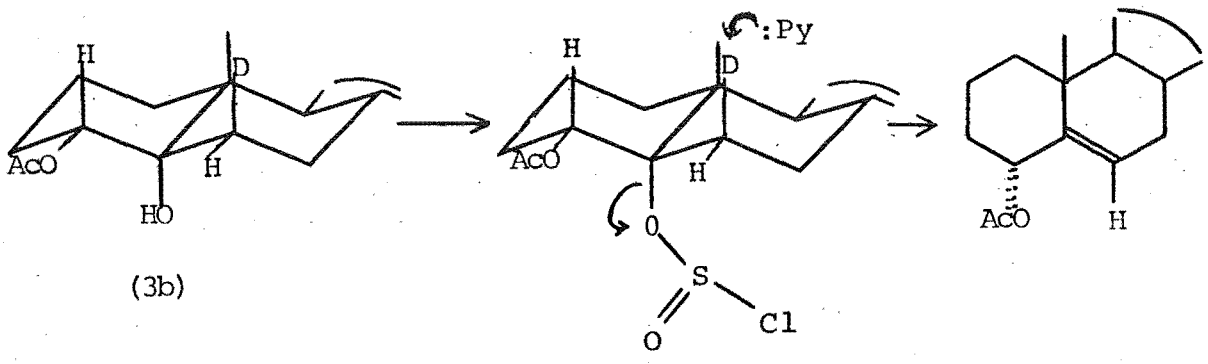


FIGURE 6.

formation of the exocyclic olefin was not dependent on the orientation of the alcohol group.[25]

The absence of rearrangement products and the preference for anti-coplanar elimination supports the view that in thionyl chloride-pyridine induced dehydration reactions proton loss occurs concurrently with C-O bond rupture. The transition state is however envisaged as being unsymmetrical, with C-O bond cleavage being more advanced than carbon-hydrogen bond rupture.

The structural simplicity and symmetry of the 8a-methyldecahydronaphthalen-4a-ol system makes it an attractive system for study of these types of reactions.

DISCUSSION

Syntheses

Of the several known routes to methyldecahydronaphthalenes the most commonly used synthesis involves Michael addition of an α,β - unsaturated ketone to a methylcyclohexanone [26]. A large number of derivatives have been prepared in this manner but the yield of products is often low[27,28]. In acidic media ring closure and dehydration are affected in a single reaction process[29]. For this study of 8a-methyldecahydronaphthalen-4a-ols, 4a-methyl-2,3,4,4a,5,6,7,8-octahydronaphthalen-2-one (19) formed from reaction between methyl vinyl ketone (20) and 2-methylcyclohexanone (21), and commercially available 8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalen-1,6-dione (22) were convenient starting materials. Removal of the C(2) and C(1)-oxy functions from 4a-methyl-2,3,4,4a,5,6,7,8-octahydronaphthalen-2-one (19) and 8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalen-1,6-dione (22) gave 8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalene (23a) and c-8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalen-r-1-ol (24a) and these substrates proved convenient intermediates for the production of a variety of oxygenated methyl-decahydronaphthalenes.

Reaction of 8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalene (23a) with monoperoxyphthalic acid gave a 2:3 mixture of *cis*- and *trans*- 1,8a-epoxy-4a-methyldecahydronaphthalenes (25a) and (26a). Attempts to separate quantities of the epoxides by preparative g.l.c., column chromatography, and high pressure liquid chromatography proved

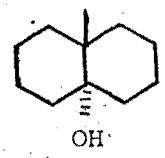
unsuccessful. Of these techniques only h.p.l.c. achieved noticeable separation, and then only on an analytical scale. Reduction of the epoxides with L.A.H. gave *cis*- and *trans*- 8a-methyldecahydronaphthalen-4a-ols (27a) and (28a) which are known compounds[27,31] and are seperable by chromatography on alumina.

To study the stereochemistry of dehydration of 8a-methyldecahydronaphthalen-4a-ols, compounds specifically labelled at C(1) were required. These were prepared by reduction of the *cis*- and *trans*-1,8a-epoxy-4a-methyldecahydronaphthalenes (25a) and (26a) with L.A.D. to give 8a-methyl-*cis*-decahydronaphthalen-r-4a-ol-t-5-*d* (27b) and 8a-methyl-*trans*-decahydronaphthalen-r-4a-ol-t-5-*d* (28b) respectively. The stereochemistry of the deuterium label for both substrates follows from the known course of reduction of epoxides with L.A.H.[32] In order to obtain a 8a-methyldecahydronaphthalen-4a-ol-5-*d* in which the deuterium label is *syn*- to the hydroxyl group it was first necessary to prepare 4a-methyl-*trans*-decahydronaphthalene-r-1,t-8a-diol (28c). This was achieved by hydrolysis of a mixture of *cis*- and *trans*- 1,8a-epoxy-4a-methyldecahydronaphthalenes (25a) and (26a) in $HClO_4$-THF-H_2O to give a seperable mixture of 4a-methyl-*trans*-decahydronaphthalene-r-1,t-8a-diol (28c) and 4a-methyl-*cis*-decahydronaphthalene-r-1,t-8a-diol (27c). The structures of the diols were determined from p.m.r. data. For diol (28c) the methyl was deshielded

by 0.2 p.p.m. relative to 8a-methyl-*trans*-decahydronaphthalen-4a-ol (28a) and the C(1)H was equatorial (δ3.48 p.p.m. $W_{\frac{1}{2}}^{h}$ 7 Hz.). For diol (27c) the methyl was deshielded by 0.02 p.p.m. relative to 8a-methyl-*cis*-decahydronaphthalen-4a-ol (27a) and the C(1)H was a broad multiplet (δ3.80 p.p.m. $W_{\frac{1}{2}}^{h}$ 14 Hz.). Oxidation of 4a-methyl-*trans*-decahydronaphthalene-r-1,t-8a-diol (28c) with chromic anhydride in pyridine afforded 8a-hydroxy-4a-methyl-*trans*-decahydronaphthalen-1-one (28d). Reduction of this ketol with L.A.D. gave 4a-methyl-*trans*-decahydronaphthalene-r-1,t-8a-diol-1-*d* (28e) identical by g.l.c. and I.R. to the undeuterated alcohol (28c). Treatment for four days with methane-sulphonyl chloride gave the corresponding 1-methanesulphonate (28f), which afforded 1,8a-epoxy-4a-methyl-*trans*-decahydronaphthalene-1-*d* (26b) on reaction with active alumina. Reduction of this epoxide with L.A.H. gave the required deuterated alcohol, 8a-methyl-*trans*-decahydronaphthalen-r-4a-ol-c-5-*d* (28g).

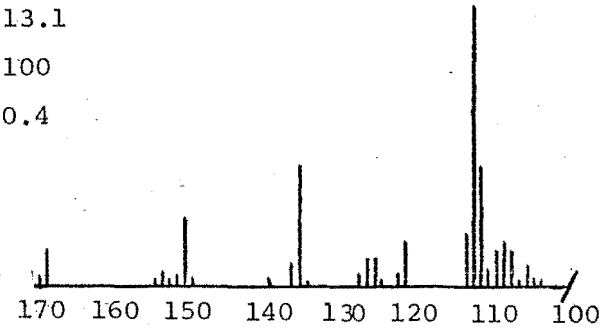
The extent of deuterium incorporation in the three labelled 8a-methyldecahydronaphthalen-4a-ols (27b), (28b) and (28g) was determined from a comparison of the mass spectra of the respective deuterated and undeuterated alcohols (fig. 7). Within experimental error 8a-methyl-*trans*-decahydronaphthalen-r-4a-ol-t-5-*d* (28b) and 8a-methyl-*cis*-decahydronaphthalene-r-4a-ol-t-5-*d* (27b) are completely deuterated. The $M^{+}+1$ and $M^{+}-1$ peaks in the mass spectrum of 8a-methyl-*trans*-decahydronaphthalen-

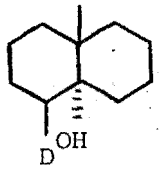
Figure 7: Mass Spectra of 8a-Methyldecahydronaphthalen-4a-ols



(28a)

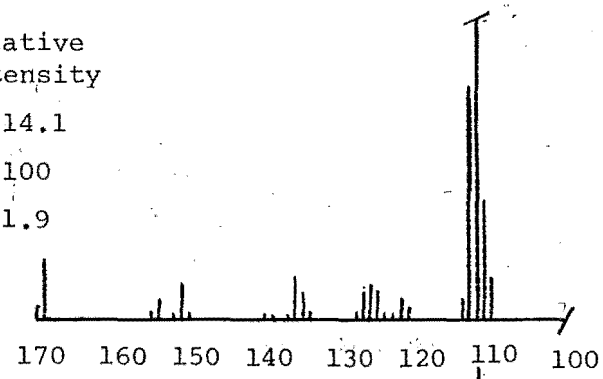
Mass	Relative Intensity
169	13.1
168	100
167	0.4

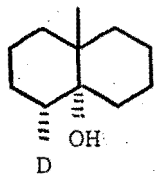




(28b)

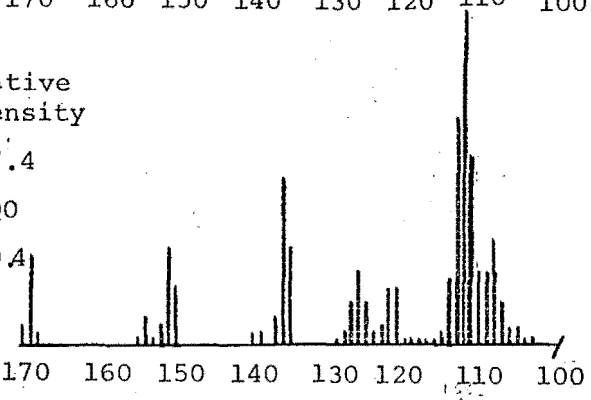
Mass	Relative Intensity
170	14.1
169	100
168	1.9

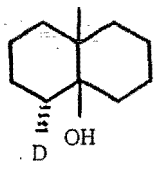




(28g)

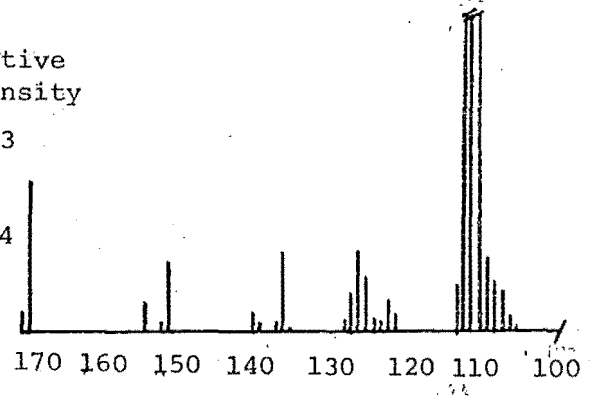
Mass	Relative Intensity
170	27.4
169	100
168	10.4

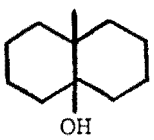




(27b)

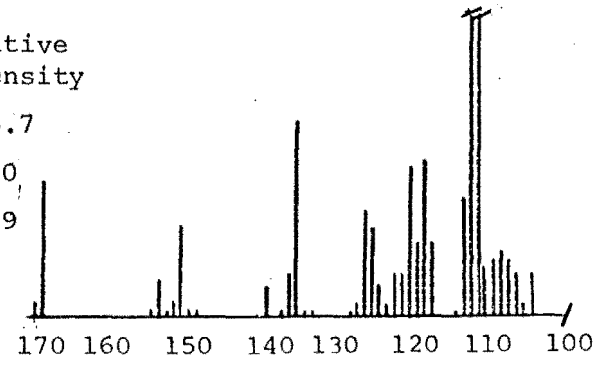
Mass	Relative Intensity
170	14.3
169	100
168	10.4





(27a)

Mass	Relative Intensity
169	13.7
168	100
167	0.9



r-4a-ol-c-5-*d* (28a), indicated the presence of 11% of dideuterated alcohol and 5.5% undeuterated alcohol in the sample. The small proportion of undeuterated alcohol is thought to result from incomplete reaction in the oxidation of diol (28c), and the second deuterium is thought to be incorporated at C(2) during L.A.D. reduction of the ketol (28d).

t-8a-Hydroxy-4a-methyl-*trans*-decahydronaphth-r-1-yl acetate (28h) was prepared by acetylation of 4a-methyl-*trans*-decahydronaphthalene-r-1,t-8a-diol (28c) with acetic anhydride - pyridine. It was not possible to obtain the monosubstituted 8a-methyldecahydronaphth-4a-yl acetates (29a) and (30a) since they rapidly lost acetic acid. Reaction of t-8a-hydroxy-4a-methyl-*trans*-decahydronaphth-r-1-yl acetate (28h) with acetyl chloride and N,N-dimethylaniline in refluxing chloroform did however give isolable quantities of 4a-methyl-*trans*-decahydro-1,8a-naphthylene diacetate (29b).

In an attempt to prepare 4a-methyl-*trans*-decahydronaphthalene-r-1,c-8a-diol (28i) and 4a-methyl-*cis*-decahydronaphthalene-r-1,c-8a-diol (27d), 8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalene (23a) was reacted with osmium tetroxide in the presence of hydrogen peroxide for 30 days.[33] Attempts to separate the diols or their mono- or diacetoxy derivatives by gas liquid, thin layer, column, and high pressure liquid chromatography were however unsuccessful.

As part of a c.m.r. study to determine the thermodynamic parameters of the interconversions between chair-chair

conformers of 4a-methyl-*cis*-decahydronaphthalenes it was of interest to synthesize 4a-methyl-*cis*-decahydronaphthalen-1-one (31a). This compound is known to be difficult to separate from the *trans*-isomer[34,35] (32a) so the problem was circumvented by separating c-4a-methyl-*cis*-decahydronaphth-r-1-yl acetate (33a) and t-4a-methyl-*trans*-decahydronaphth-r-1-yl acetate (34a) prepared by hydroboration - oxidation of 8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalene (23a) followed by acetylation of the resulting isomeric alcohols. Reduction of the *cis*- acetate (33a) with L.A.H. and oxidation of the resulting alcohol (33b) with CrO_3-pyridine in methylene chloride[37] gave the required 4a-methyl-*cis*-decahydronaphthalen-1-one (31a).

Conformational Studies

Since the postulation of the tetrahedral carbon, decahydronaphthalene and its derivatives have been important in organic chemistry. As early as 1890 Sachse[38,39] proposed the existence of several conformers of *cis*- and *trans*-decahydronaphthalene (35) and (36). Some time after this Mohr[40,41] proposed that at ambient temperatures chair and boat forms of cyclohexane underwent rapid interconversion, which if true meant that there would only be two isolable isomers of decahydronaphthalene. The experimental studies of Bastiansen and Hassel[42] in 1946, using electron diffraction techniques showed that the ground state for *cis*-decahydronaphthalene

(35) contained both rings in a chair conformation. Turner[43-45] accounted for the observed differences in energy between *cis*- and *trans*-decahydronaphthalene in terms of the number of "gauche-butane" like interactions for each isomer. Using a combination of experimental and calculative proc edures Gerig and Roberts[46] proposed an energy profile for the interconversion of the chair-chair enantiomorphs of *cis*-decahydronaphthalene (35). However the early n.m.r. techniques used by Roberts and Gerig[46] required the molecule under study to be substituted extensively with deuterium or fluorine. The advent of c.m.r. spectroscopy has removed many of the difficulties associated with the determination of thermodynamic parameters by proton or fluorine-19 magnetic resonance. With the C-13 method molecules can be examined directly without the need for extensive deuteration, and the presence often of more than one equilibrating resonance in the molecule provides corroborative data. The difference in chemical shifts between carbon resonances in interchanging conformational environments is often large, allowing measurements to be made over a wide temperature range. This is necessary if entropy factors are to be determined with any accuracy.

In this study the thermodynamic parameters of two equilibrating *cis*-decahydronaphthalene systems have been determined by lineshape analysis of their c.m.r. spectra over a range of temperatures. The systems chosen were 8a-methyl-*cis*-decahydronaphthalen-4a-ol (27a), equilibrating between enantiomers (37) and (38), and 4a-methyl-

cis-decahydronaphthalen-1-one (31a), equilibrating between conformers (39) and (40) (fig. 8). The 4a-methyl-*cis*-decahydronaphthalen-1-one (31a) system is of particular interest as previous attempts to determine which conformation is the more stable are in disagreement.[47,67,68] C.m.r. lineshape analysis offers a method of unambiguously resolving this problem.

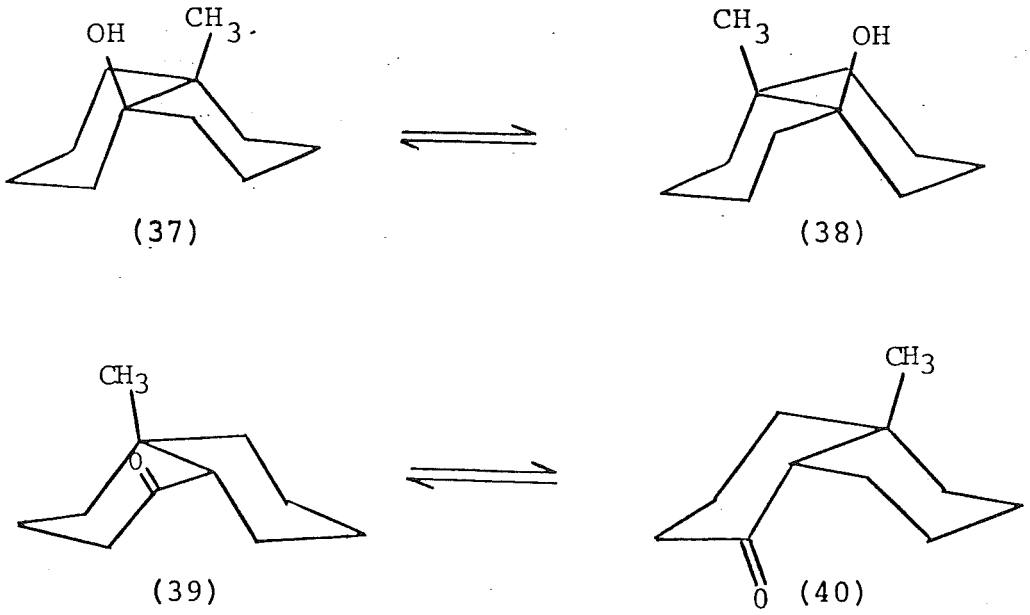


Figure 8.

Lineshape analysis has been used to study the conformational equilibrium process A ⇌ B where A and B are different conformational enantiomorphs of an organic molecule and at least one carbon atom is exchanging between chemically non-equivalent positions.[48] If

the lifetime of a carbon atom in each position is long relative to the n.m.r. timescale, the spectra for the individual conformers can be recorded. If however the lifetime of the conformers is relatively short, a single spectrum in which the chemical shifts are statistically weighted averages of the corresponding values for the exchanging species will be obtained.

The classical equations describing the magnetization of a nucleus in an external magnetic field in terms of the precession of nuclear magnetic dipoles have been formulated by Bloch[49]. Early applications of the Bloch equations to the problem of a nucleus exchanging between two non-identical sites were somewhat involved, and have since been simplified[50,51]. For this study the equations referred to by Binsch[48] were used. If it is assumed that both the forward and reverse processes in the equilibrium can be described by first order kinetic rate laws the Bloch equations can be modified to produce an expression for the calculation of the complete n.m.r. line shape over the whole spectral sweep range as a function of the parameters ν_A, ν_B, T_{2A}, T_{2B}, p_A, p_B and τ[48]. The chemical shifts ν_A and ν_B of the exchanging carbons are obtained by direct measurement from the low temperature below coalescence spectrum. The transverse relaxation times T_{2A} and T_{2B} are replaced by the value T_2^* which is derived from the equation $T_2^* = \frac{1}{\pi\omega}$ where ω is the width in Hertz at half height of a peak not broadened by exchange. This is a satisfactory approximation provided

care is taken to keep field imhogeneities to a minimum while recording the spectrum. Where no such peaks occur ω may be determined by using an internal reference compound such as TMS. The population parameters p_A and p_B are equal when the equilibrium is between energetically equivalent conformations. When dealing with equilibrating species of differing energy p_A and p_B may be determined by measuring the integrals of peaks due to each conformer in the low temperature spectrum, or by reference to other data such as p.m.r. spectra. Where an approximate value only is known, p_A and p_B may be treated as limited free parameters. The variable τ is related to the lifetimes of A and B by the equation

$$\tau = \tau_A p_B = \tau_B p_A \quad ,$$

where the lifetimes of A and B (τ_A and τ_B) are the reciprocals of the rate constants, $k_{A\rightarrow B}$ and $k_{B\rightarrow A}$ respectively, for the equilibration process[48].

For this study c.m.r. spectra were recorded on a Varian CFT-20 spectrometer equipped with a Sykes Compucord system. A subroutine was written and incorporated into the CFT-20 software for the calculation of the total transverse magnetization, G, using the expression given by Binsch*[48]. With τ as a variable measured or

* $$G = \frac{-iC\tau[\,2p_A - p_B - \tau(p_A\alpha_B + p_B\alpha_A)]}{p_A p_B - \tau^2\alpha_A\alpha_B}$$

where $$\alpha_A = -[\,2\pi i(\nu_A - \nu) + 1/T_{2A} + p_B/\tau]$$

and $$\alpha_B = -[\,2\pi i(\nu_B - \nu) + 1/T_{2B} + p_A/\tau]$$

and $$C = \gamma H_1 M_0$$

estimated values of the other parameters were fed into this program, and the calculated lineshapes compared with the recorded spectra. Time was saved in refining the data by displaying the calculated spectra on the CFT 20 oscilloscope. When it appeared that a simulated spectrum closely approximated a recorded spectrum the simulated spectrum was recorded and compared with the authentic spectrum. In all cases a variation of 10% in the value of τ from that value required to produce a visual best fit produced a clearly non-optimal simulation. The methods used for determining the thermodynamic parameters have a very low sensitivity to changes of this magnitude for any given value of τ. The direct relationship between τ and reaction rates k_r for the equilibration processes enables the thermodynamic parameters Ea, $\Delta H^{\ddagger}$, and $\Delta S^{\ddagger}$, to be determined relative to k_r.

The activation energy for an equilibration is related to reaction rate by the Arrhenius equation.

$$k_r = Ae^{\left(-\frac{E_a}{RT}\right)}$$

Construction of a plot of lnk *vs.* $-\frac{1}{RT}$ gives a line of slope Ea. The enthalpy $\Delta H^{\ddagger}$ and entropy $\Delta S^{\ddagger}$ may be determined from the Eyring equation,

$$k_r = \kappa\left(\frac{kT}{h}\right)e^{(\Delta S^{\ddagger}R)}e^{(-\Delta H^{\ddagger}/RT)} \quad .$$

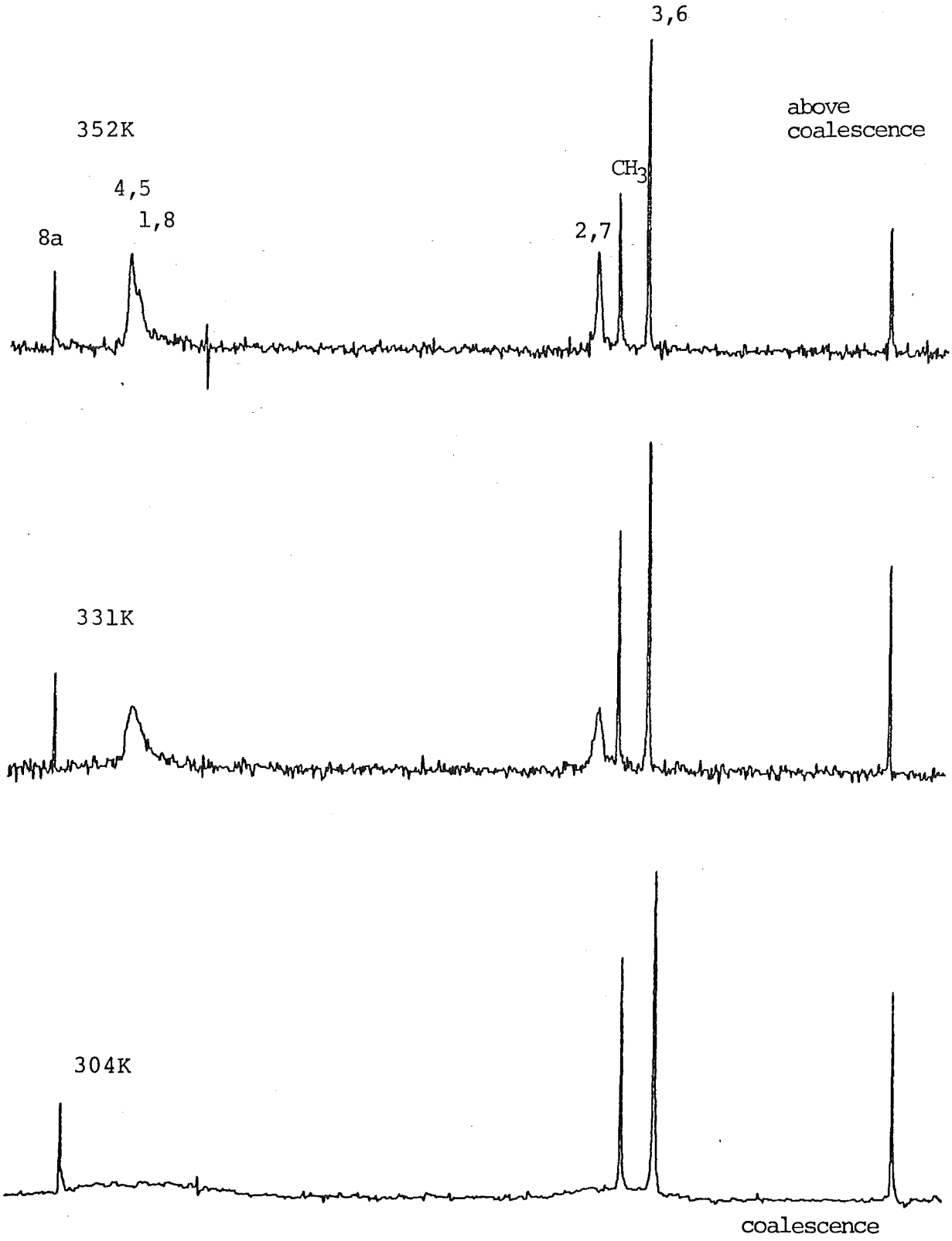
Plotting $-R\ln\left(\frac{hk_r}{kT\kappa}\right)$ against $\frac{10^3}{T}$ gives a line of slope

$\Delta H^{\ddagger}$ with intercept $-\Delta S^{\ddagger}$. In this study the values were calculated by linear least squares analysis.

Spectra of 8a-methyl-*cis*-decahydronaphthalen-4a-ol (27a) as a neat liquid were obtained at fifteen points in the temperature range 266.0 to 352.4K. At temperatures in excess of ambient rapid interchange of the two energetically equivalent chair-chair conformers (37) and (38) reduced the number of lines in the proton noise decoupled spectrum to seven. As the temperature was lowered to 304K spectral lines due to carbons exchanging between non equivalent positions broadened. Below the coalescence temperature the spectrum resolved into eleven lines, allowing the unique chemical shift of each carbon in the conformers (37) and (38) to be observed. These trends are seen in the selected spectra shown in fig. 9.

Spectral assignments were made as follows. The assignment for C(4a) was made on the basis of the large hydroxyl substituent effect. The other non-exchanging carbons, the methyl carbon and C(8a), are well separated allowing unambiguous assignment. The methylene carbons were assigned by comparison of the recorded spectra with calculated values (table I). These were obtained by adding to the known low temperature chemical shifts for 4a-methyl-*cis*-decahydronaphthalene[52], the known effect of an axial or equatorial hydroxyl substituent in cyclohexane[53] as appropriate. In conformation (37) the hydroxyl substituent is axial to ring A and equatorial to ring B, while in conformation (38) the reverse applies.

8a-Methyl-cis-decahydronaphthalen-4a-ol



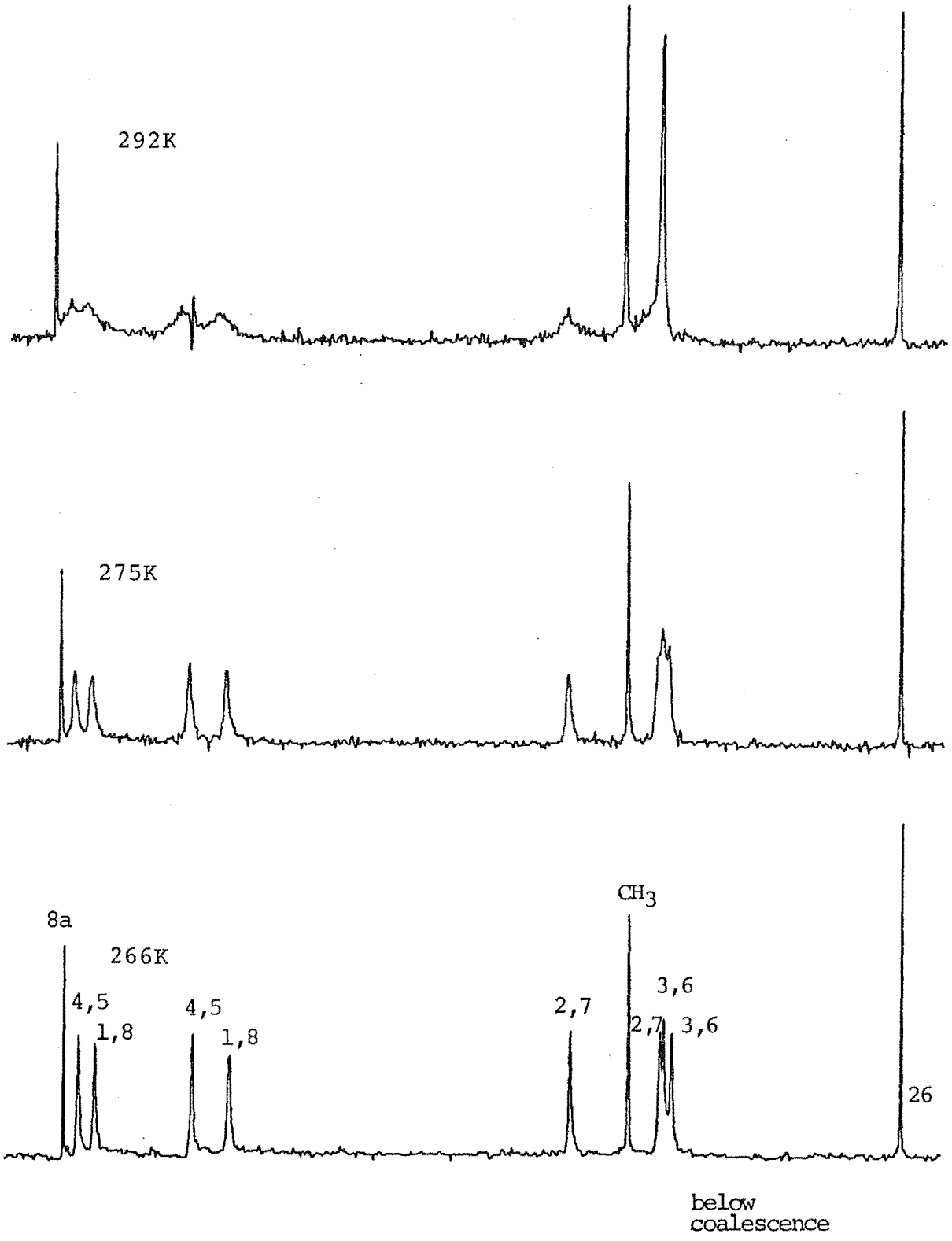


Figure 9 Continued.

TABLE 1

Carbon-13 Chemical Shift Data[a] for 8a-methyl-*cis*-decahydronaphthalen-4a-ol (27a).

Carbon	Calc.[b]		obs.[c]		
			(238 K)		(352 K)
1,8	35.5	29.3	36.3_1	32.4_3	35.9_5
2,7	22.1	21.2	23.8_1	21.5_7	23.5_9
3,6	21.2	20.7	21.3_5	21.0_9	22.2_8
4,5	33.6	36.3	33.6_3	36.4_5	36.1_2
4a			73.5_1		73.4_8
8a			37.1_6		38.1_6
CH_3			22.4_2		23.0_0

a p.p.m. relative to TMS = 0 p.p.m

b see text

c ± 0.05 p.p.m.

No corrections have been made for buttressing effects in the calculated spectrum, and this probably accounts for the differences of greater than 1.0 p.p.m. between the predicted and observed values for some of the carbons. These assignments are supported by the fact that the above coalesence spectra can be generated from the below coalescence spectra only if the pairings made for the conformationally interchanging carbons are correct.

Generation of simulated spectra requires values for parameters p_A, p_B, T_2^*, ν_A, ν_B and τ. In this case the energy equivalence of conformers (37) and (38) implies $p_A = p_B = 0.5$. The transverse relaxation times were estimated from the width at half height of the C(10) and CH_3 spectral lines at each temperature. The frequencies of the interchanging pairs, measured directly from the below coalescence spectra, were found to vary slightly with temperature and therefore values for simulations above coalescence temperatures were obtained by extrapolation of a plot of ν *vs.* T for each carbon. The values of τ were found from the simulation studies.

Thermodynamic parameters were calculated from a linear least-squares analysis of the Arrhenius and Eyring functions, with values of $\frac{1}{T}$ and τ as input to the computer as in Table V, p 37. The errors reported are statistical errors. The largest source of experimental error probably results from temperature fluctuations in the spectrometer during data accumulation. To minimize this error, two

points were included for each rate constant, representing the temperature recorded before and after the accumulation of data at each set temperature. The statistical error given will largely reflect the experimental error.

The Eyring equation contains a term κ, the transmission coefficient, in the entropy determining expression. The assumption of Dalling, Grant, and Johnson[54], that the rate determining step in the equilibration of the conformers of 4a-methyl-*cis*-decahydronaphthalene involves an intermediate which may leave its potential well in either direction is considered appropriate for 8a-methyl-*cis*-decahydronaphthalen-4a-ol. The transmission coefficient κ of 0.5 is therefore used in the calculation of the entropy.

The thermodynamic parameters obtained from the rate data for equilibration between conformers (37) and (38) of 8a-methyl-*cis*-decahydronaphthalen-4a-ol (27a) were;

$$E_a = 69.8 \pm 0.9 \text{ kJmol}^{-1}$$

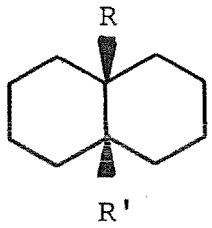
$$\Delta H^{\ddagger} = 66.7 \pm 1.3 \text{ kJmol}^{-1}$$

$$\Delta S^{\ddagger} = +12 \pm 5 \text{ JK}^{-1}\text{mol}^{-1}.$$

The activation energies found in this study are lower than those obtained by Altman *et al.*[55] for a series of 4a,8a- disubstituted *cis*-decahydronaphthalenes, however the enthalpy is greater than the values reported for

TABLE II

Thermodynamic Parameters for Conformational Inversion of Substituted *cis*-Decahydronaphthalenes.



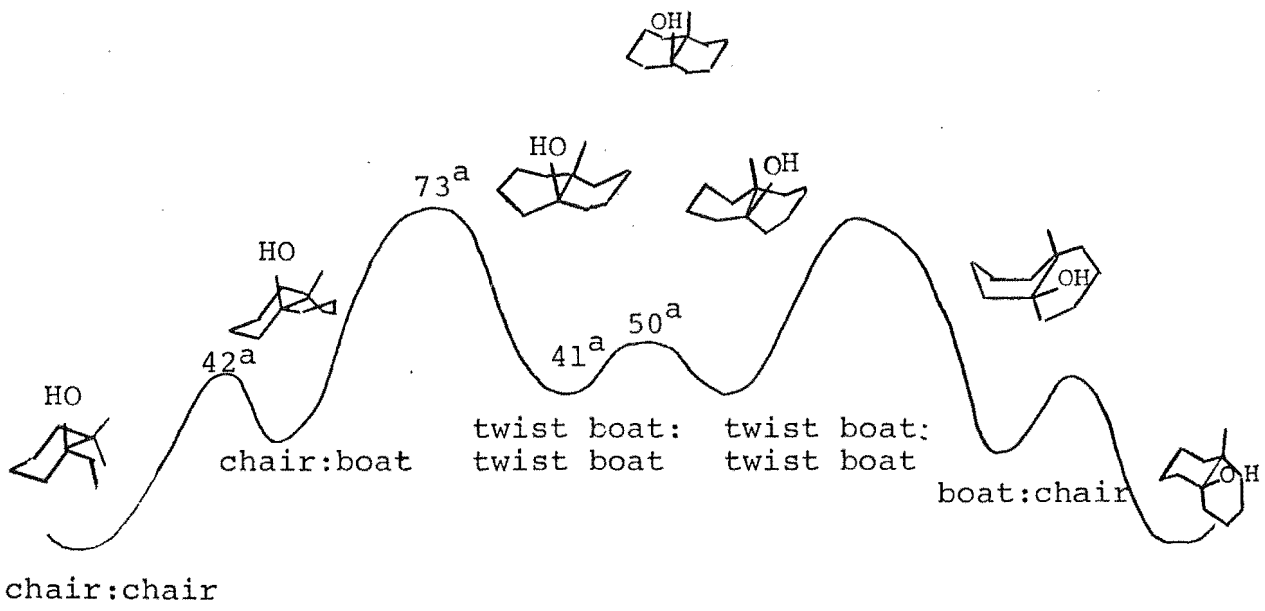
R = R' = $CH_2CO_2CH_3$	Ea^a = 86.2 ± 2.5 $kJmol^{-1}$	
R = R' = CH_2Br	Ea^a = 78.2 ± 5 $kJmol^{-1}$	
R = CH_3, R' = CH_2Br	Ea^a = 75.3 ± 5.9 $kJmol^{-1}$	
R = CH_3, R' = CH_2CN	Ea^a = 77.4 ± 2.9 $kJmol^{-1}$	
R = CH_3, R' = H	$\Delta H^{\ddagger b}$ = 51.9 $kJmol^{-1}$	$\Delta S^{\ddagger}$ = 2.93 ± 12.5 $JK^{-1}mol^{-1}$
R = R' = H	$\Delta H^{\ddagger}$ = 56.9 $kJmol^{-1}$	$\Delta S^{\ddagger}$ = 14.6 ± 12.5 $JK^{-1}mol^{-1}$
R = CH_3, R' = OH	Ea = 69.8 ± 0.9 $kJmol^{-1}$	
	$\Delta H^{\ddagger}$ = 66.7 ± 3 $kJmol^{-1}$	$\Delta S^{\ddagger}$ = 12 ± 5 $JK^{-1}mol^{-1}$

(a) Ref. 55

(b) Ref. 54

cis-decahydronaphthalene and *cis*-methyldecahydronaphthalene[54] (table II). Superficially these trends might be thought to be due to the degree of steric interaction resulting from eclipsing of the C(4a) and C(8a) substituents during conformational interconversion *via* an eclipsed bridgehead transition state. Gerig and Roberts[46,47] have calculated the potential energy for several conformations of *cis*-decahydronaphthalene using Wiberg's method[56] and concluded that conformational inversion involves the sequence chair:chair - chair:twist boat - twist boat: twist boat - twist boat^1:twist boat^1 - twist boat^1:chair - chair^1:chair^1 (fig. 10). By adding the experimental value for the energy barrier for cyclohexane inversion to the values calculated for conformations in which at least one ring was in the chair form they were able to obtain estimates for the energies of the transition states for conformational changes involving chair-boat interconversion. From a comparison of these calculated transition state energies with the energy of the eclipsed bridgehead transition state for interconversion of the two twist boat:twist boat conformers, they found the rate determining step for conformational inversion of the chair:chair forms of *cis*-decahydronaphthalene to be the transition between the chair:twist boat and twist boat:twist boat conformations (fig. 10). From microwave studies, the barrier to hindered methyl rotation for gauche 1-propanol has been determined to be 12.9±0.2 kJmol^{-1} in the gas phase.[57] The values determined for propane[58] and ethane[59,60] are 13.9±0.08 kJmol^{-1}

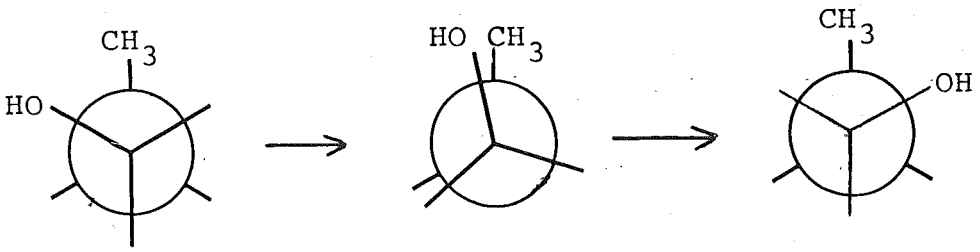
Conformational Inversion
of
8a-Methyl-*cis*-decahydronaphthalen-4a-ol



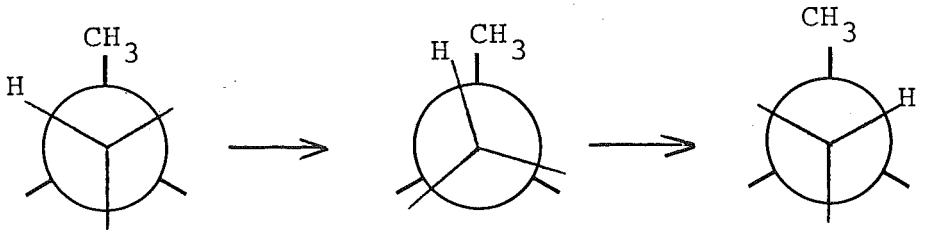
a Estimated[46] energies of intermediates and transition states for *cis*-decahydronaphthalene in $kJmol^{-1}$, relative to the chair:chair form.

Figure 10.

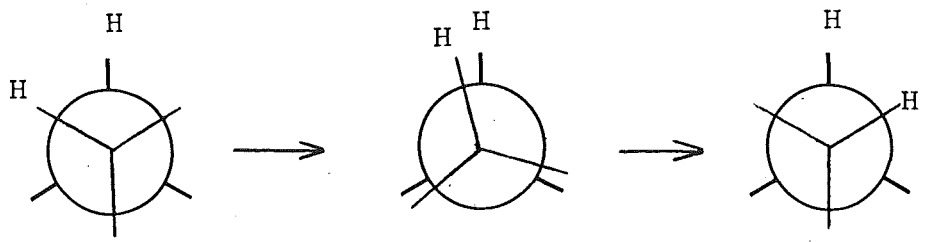
and 11.7-12.7 kJmol^{-1} respectively (fig. 11).



12.9 ± 0.2 kJmol^{-1}



13.9 ± 0.08 kJmol^{-1}



11.7 - 12.7 kJmol^{-1}

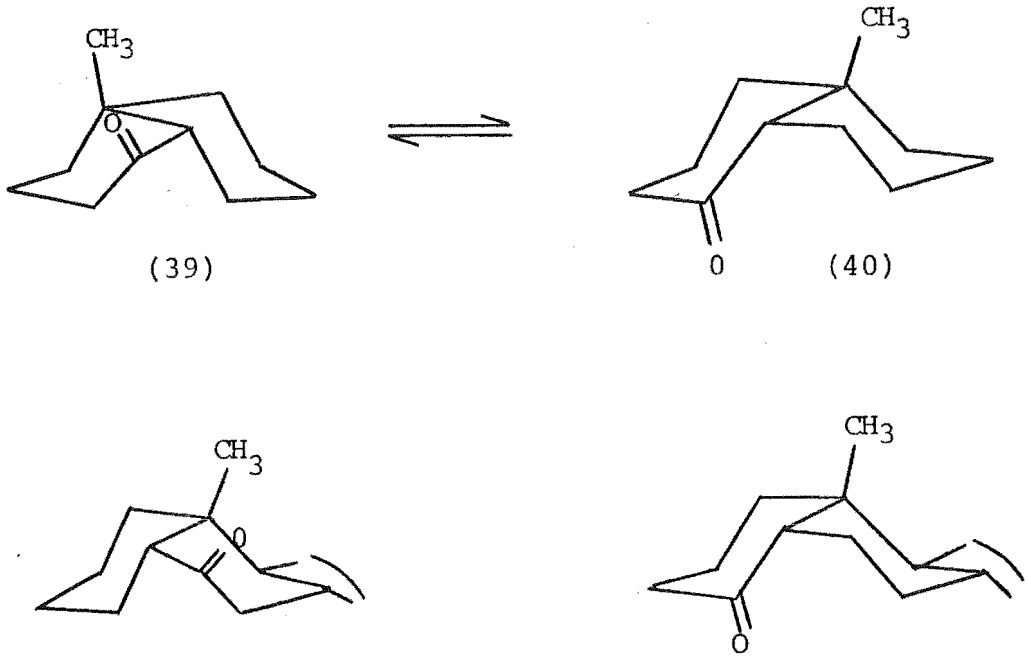
Figure 11.

If the assumption is made that these conformational energy barriers are similar in solution, then the difference in activation energy and enthalpy for conversion of the optical enantiomorphs of *cis*-decahydronaphthalene (35),4a-methyl-*cis*-decahydronaphthalene

(33c), and 8a-methyl-*cis*-decahydronaphthalen-4a-ol (27a), cannot be attributed solely to an increase in energy of the transition state between the twist boat: twist boat conformations resulting from eclipsing of the C(4a) and C(8a) substituents, and may be due to more complex interactions in the molecule. The differences in energy barriers to rotation as shown in fig. 11 are too small to account for the differences in activation energy observed for the above *cis*-decahydronaphthalenes, but the transition state between the twist boat:twist boat conformers may become rate determining when the substituents are bulky (e.g. first two compounds in table II).

The c.m.r. spectra of 4a-methyl-*cis*-decahydronaphthalen-1-one (31a) in $CDCl_3$ were recorded at nine points in the temperature range 200.5 K to 288.1 K. The below coalescence spectra showed the molecule to exist in two unequally populated conformations (39) and (40) (fig. 12). The peaks could be readily assigned to the conformers on the basis of relative intensity. Integration of the c.m.r. peaks at δ59.1 p.p.m. and δ54.0 p.p.m. gave an approximate population ratio of 0.65:0.35. In order to assign the c.m.r. spectra it was first necessary to establish which conformer of 4a-methyl-*cis*-decahydronaphthalen-1-one (31a) was dominant. This was achieved by variable temperature p.m.r. studies. The p.m.r. spectrum of 4a-methyl-*cis*-decahydronaphthalen-1-one (31a) was recorded at fifteen points in the temperature range 178-288K. Above coalescence temperature (206 K)

the methyl resonance appeared as a singlet at δ0.98 p.p.m., but on cooling two methyl resonances appeared, at δ0.90 and δ1.15. An estimate of 0.66:0.34 for the population ratio was obtained from the relative positions of the above and below coalescence methyl resonances. The resonance at δ0.90 was found to be associated with the dominant conformer. The p.m.r. spectrum was assigned on the basis of the structural similarity of conformation (39) of 4a-methyl-*cis*-decahydronaphthalen-1-one to coprostan-6-one (41) and conformation (40) to coprostan-4-one (42) (fig. 12). By analogy with the chemical shift of the



(39) (40)

(41) (42)

Figure 12.

C(10)-methyl in the p.m.r. spectra of coprostan-6-one[61] (41) and coprostan-4-one[62] (42), calculated values of δ0.91 and δ1.15 were obtained for the chemical shift of the methyl resonance in conformations (39) and (40) respectively of 4a-methyl-*cis*-decahydronaphthalen-1-one (31a). Conformer (39) is therefore the more stable conformer.

Knowing the dominant conformer from the p.m.r. study the assignment of the below coalescence c.m.r. spectrum was simplified and was made by reference to the c.m.r. spectra of coprostan-6-one (41) and coprostan-4-one (42), which were in turn assigned from the c.m.r. spectrum of coprostane[63] (43) and the known effect of a ketone substituent in 4a-methyl-*trans*-decahydronaphthalen-1-one (32a). The change in chemical shifts of the ring C and D and side chain carbons by the introduction of a C(4) or C(6) carbonyl moiety into coprostane was assumed to be minimal. Values for the resonances of carbons in the rings containing the carbonyl moiety were estimated from the known effects of a C(1) carbonyl on the carbon resonances of 4a-methyl-*trans*-decahydronaphthalene (34b) (table III). The remaining signals could be assigned from chemical shift and carbon-hydrogen couplings.

From the observed values for the coprostanones (41) and (42), the experimental effect on the ring A and ring B carbons of coprostane by introducing a carbonyl function at C(6) or C(4) could be determined, and this shift data was used to assign the c.m.r. spectra of

TABLE III

Carbon-13 Chemical Shifts[a] of Coprostane(40), Coprostan-4-one (38) and Coprostan-6-one (39).

Carbon	Coprostane[b]	Coprostan-4-one			Coprostan-6-one		
		calc.[c]	obs.[d]	e	calc[c]	obs[d]	e
1	37.9	36.6	35.2_1	-2.7		37.1_0	-0.8
2	21.7	20.1	20.1_0	-1.6		20.6_4	-1.1
3	27.5	41.0	41.4_9	+14.0		25.5_7	-1.9
4	27.9		f			26.5_6	-1.3
5	44.2	56.0	56.2_5	+12.1	56.0	61.1_5	+17.0
6	27.6		20.2_8	-7.3		f	
7	26.9		27.5_3	+0.6	40.5	39.8_1	+12.9
8	36.2		35.7_8	-0.4	34.6	35.7_3	-0.5
9	40.7		44.1_1	+3.4	39.4	43.0_6	+2.4
10	37.7		40.5_5	+2.9	43.4	38.3_2	+0.6
11	21.1		20.9_0			20.9_1	
12	40.6		39.8_7			40.0_0	
13	43.0		42.4_6			43.0_6	
14	57.0		57.1_3			57.0_0	
15	24.5		24.1_7			24.1_2	
16	28.6		28.2_5			28.1_4	
17	56.8		56.2_5			56.2_4	
18	12.1		11.9_2			11.9_8	
19	24.4		23.1_4	-1.3		24.0_5	-0.3
20	36.1		36.1_5			36.1_0	
21	18.8		18.6_7			18.6_7	
22	36.5		36.4_8			36.1_0	
23	24.1		23.8_6			23.8_4	
24	39.8		39.5_2			39.5_1	
25	28.3		27.9_9			28.0_6	
26	22.8		22.8_0			22.8_2	
27	22.6		22.5_5			22.5_7	

a p.p.m relative to TMS = 0 p.p.m.

b values taken from ref. 63.

c see text

d ± 0.05 p.p.m.

e δ obs - δ coprostane

f resonance not measured

TABLE IV

Carbon-13 Chemical Shift Data[a] for 4a-methyl-*cis*-decahydronaphthalen-1-one (31a)

	Conformer (39) (200 K)		Conformer (40) (288K)	Conformer (40) (200 K)	
Carbon	Calc[b]	Obs[c]	Obs	Calc[b]	Obs[c]
2	34.7	36.7_8	38.5_4	41.8	41.8_0
3	22.3	21.1_2	21.4_9	21.2	21.1_2
4	32.8	28.1_3	32.8_1	39.6	39.6_2
5	41.5	38.8_7	37.0_9	33.8	32.5_3
6	21.6	21.6_9	21.6_4	22.4	21.6_9
7	25.9	25.2_4	24.1_3	22.4	21.3_0
8	26.8	26.6_7	24.6_3	21.1	20.2_7
9	58.8	59.1_1	57.6_0	53.9	54.0_0
10	33.7	36.2_1	37.0_4	36.0	38.7_0
CH_3	27.7	27.9_6	27.9_9	27.0	27.9_6

a p.p.m. relative to TMS = 0 p.p.m.

b calculated using δ values (Table II) from 4a-methyl-*cis*-decahydronaphthalene (34b).

c ± 0.05 p.p.m.

d carbonyl chemical shift not measured.

4a-methyl-*cis*-decahydronaphthalen-1-one (31a) in conformations (39) and (40) (Table IV). The matching of the calculated and observed values was helped by the unequal population of the two conformers.

The chemical shifts of the below coalescence spectra were found to vary only slightly with temperature, and so no corrections were made to below coalescence line positions when simulating above coalescence spectra. Values for T_2^* were derived from the width of half height of the reference TMS signal, as there was no suitable non-exchanging carbon in the 4a-methyl-*cis*-decahydronaphthalen-1-one (31a) spectra. The population parameters p_A and p_B had been measured approximately by integration of the c.m.r. peaks at δ54.0 (C(9) conformer (40)) and δ59.1 (C(9) conformer (39)) and from the p.m.r. spectral data (CH_3 conformer (39), δ0.90; CH_3 conformer (40), δ1.15; CH_3 time averaged spectrum, δ0.98) as 0.66:0.34. This ratio was treated as a limited free parameter in the simulations. A value of 0.68:0.32 was found to allow the best simulation at 200.1 K, but a gradual change to 0.65:0.35 was necessary as higher temperature spectra were simulated.

Thermodynamic data were determined from the rate parameters (table V), and for the equilibrium (39) ⇌ (40) the following values were determined;

$E_a = 42.9 \pm 0.7\ kJmol^{-1}$.

$\Delta H^{\ddagger} = 41.0 \pm 0.7\ kJmol^{-1}$.

$\Delta S^{\ddagger} = 41.0 \pm 3JK^{-1}\ mol^{-1}$.

INPUT DATA

Y	X
667E+01	+2868E-01
667E+01	+2881E-01
692E+00	+2702E-01
692E+00	+2716E-01
333E+00	+2623E-01
333E+00	+2623E-01
000E+00	+2509E-01
000E+00	+2538E-01
556E-01	+2392E-01
556E-01	+2407E-01
100E+00	+2239E-01
100E+00	+2235E-01
857E-02	+2106E-01
857E-02	+2108E-01
125E-01	+2056E-01
125E-01	+2056E-01
010E+00	+2005E-01
010E+00	+2005E-01

ARRHENIUS PLOT OF

LNK VS -1000/RT

DATA FOR LEAST SQUARES ANALYSIS

+9721E-03	-4194E-04
+9721E-03	-4175E-04
+8947E-03	-4452E-04
+8947E-03	-4429E-04
+8111E-03	-4586E-04
+8111E-03	-4588E-04
+7600E-03	-4794E-04
+7600E-03	-4740E-04
+6320E-03	-5029E-04
+6320E-03	-4998E-04
+4605E-03	-5373E-04
+4605E-03	-5382E-04
+3352E-03	-5712E-04
+3352E-03	-5706E-04
+2525E-03	-5851E-04
+2525E-03	-5851E-04
+2302E-03	-5999E-04
+2302E-03	-5999E-04

Y CALC	Y DEV
+9845E-03	+1237E-04
+9926E-03	+2050E-04
+8738E-03	-2091E-04
+8837E-03	-1106E-04
+8163E-03	+5158E-05
+8163E-03	+5158E-05
+7268E-03	-3323E-04
+7503E-03	-9710E-05
+6261E-03	-5824E-05
+6386E-03	+7630E-05
+4786E-03	+1812E-04
+4745E-03	+1400E-04
+3329E-03	-2259E-05
+3353E-03	+6866E-07
+2733E-03	+2076E-04
+2733E-03	+2076E-04
+2094E-03	-2081E-04
+2094E-03	-2081E-04

STANDARD DEVIATION OF RESIDUALS = +1668E-04

EA(KJ/MOL)= +4293E-02
ERROR = +6329E-04

LNA = +2785E-02
ERROR = +3253E-04

ACTIVATION PARAMETERS FROM PLOT OF -RLN(KRH/KT) V 1000/T

DATA FOR LEAST SQUARES ANALYSIS

+1637E-01	+3486E-03
+1638E-01	+3471E-03
+1696E-01	+3700E-03
+1697E-01	+3681E-03
+1764E-01	+3812E-03
+1764E-01	+3812E-03
+1802E-01	+3985E-03
+1803E-01	+3940E-03
+1905E-01	+4180E-03
+1905E-01	+4154E-03
+2042E-01	+4486E-03
+2042E-01	+4474E-03
+2141E-01	+4748E-03
+2141E-01	+4743E-03
+2208E-01	+4863E-03
+2208E-01	+4863E-03
+2224E-01	+4987E-03
+2224E-01	+4987E-03

Y CALC	Y DEV
+1626E-01	-1113E-03
+1620E-01	-1795E-03
+1714E-01	+1728E-03
+1706E-01	+9044E-04
+1759E-01	-4106E-04
+1759E-01	-4106E-04
+1830E-01	+2809E-03
+1812E-01	+3482E-04
+1910E-01	+5448E-04
+1900E-01	-5745E-04
+2027E-01	-1459E-03
+2031E-01	-1117E-03
+2143E-01	+1905E-04
+2141E-01	-1938E-06
+2190E-01	-1752E-03
+2190E-01	-1752E-03
+2241E-01	+1671E-03
+2241E-01	+1671E-03

STANDARD DEVIATION OF RESIDUALS = +1392E-03

ACTIVATION ENTHALPY (KJ/MOL) = +4097E-02
ERROR = +6352E-04

(-)ACTIVATION ENTROPY (J/K/MOL) = +1979E-02
ERROR = +2715E-03

The difference in free energy between conformers (39) and (40) may be determined from the equation

$$\Delta G = -RT\ln K.$$

where K is the population ratio of the conformers. From the known population ratio at 200.1 K conformer (40) was determined to be 1.25 $kJmol^{-1}$ higher in energy than conformer (39). The errors quoted are statistical errors and two points representing the probe temperature before and after data collection were plotted for each rate parameter.

If conformational inversion takes place by a sequence analogous to that proposed by Gerig and Roberts[46] for *cis*-decahydronaphthalene rapid inversion of the more flexible carbonyl containing ring would be expected to be followed by slower inversion of the second ring, as in fig. (13). The barrier to conformational inversion of cyclohexanone[65] is reported as 11.7-13.8 $kJmol^{-1}$, which is *ca.* 9 $kJmol^{-1}$ less than for cyclohexane[66]. If inversion of the cyclohexanone ring in 4a-methyl-*cis*-decahydronaphthalen-1-one occurs in the rate determining step for the interconversion (39) → (40), then the difference in energy between the ground and transition states for 4a-methyl-*cis*-decahydronaphthalen-1-one would be expected to be approximately 9 $kJmol^{-1}$ less than for the analogous

Conformational Inversion of

4a-methyl-*cis*-Decahydronaphthalene

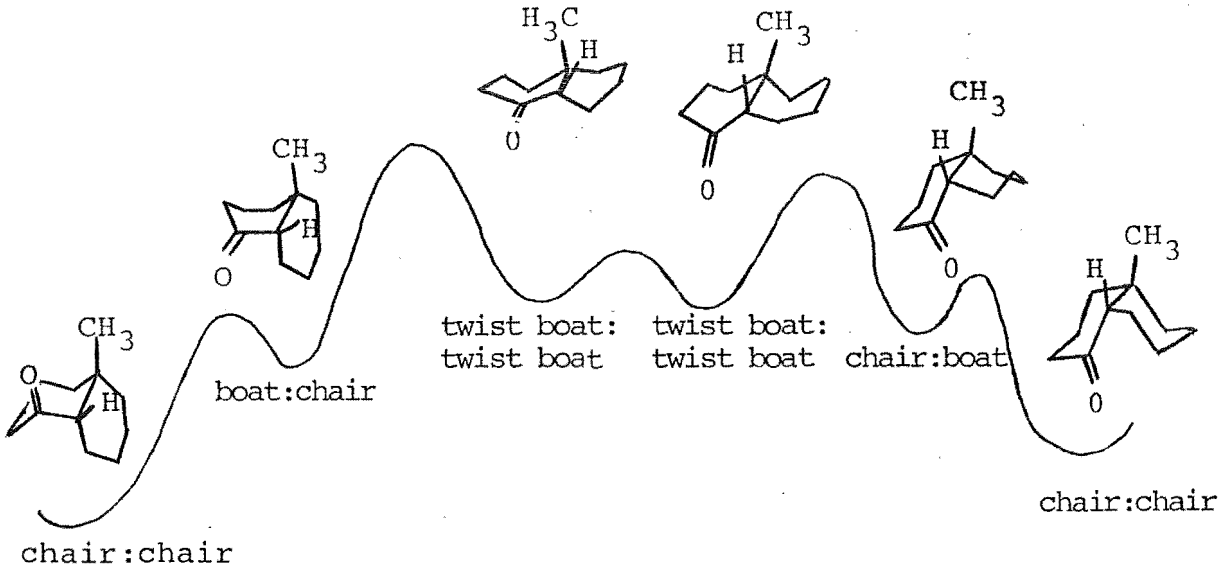


Figure 13.

process in 4a-methyl-*cis*-decahydronaphthalene. The difference in enthalpy of inversion of 4a-methyl-*cis*-decahydronaphthalen-1-one and 4a-methyl-*cis*-decahydronaphthalene[54] is 10.9 $kJmol^{-1}$, supporting this simplistic analysis. Previous attempts have been made to predict the favoured conformer in the equilibration of 4a-methyl-*cis*-decahydronaphthalen-1-one. Klyne[67] predicted conformer (39) to be more stable by *ca.* 4$kJmol^{-1}$ on the basis of simple first order analysis of the interactions present. This value was supported by the O.R.D. measurements of Djerassi and Marshall.[68] Force-field calculations led Allinger *et al.*[47]

to predict that conformer (40) would be more stable by 0.46 $kJmol^{-1}$. The low temperature c.m.r. method employed in this study allows unambiguous assignment of the more stable conformer as (39). While this confirms the earlier assignments of Klyne[67] and Djerassi[68], in quantitative terms the more recent energy calculations of Allinger[47] are more accurate.

C.m.r. spectra of substituted methyldecahydronaphthalenes

The effects of a substituent on the c.m.r. spectra of decahydronaphthalenes and related compounds have been discussed in terms of the α,β,γ,δ,ε and ξ substituent effects. These refer to the change in chemical shift on the introduction of a substituent of the resonances of carbons separated from the substituent by 1,2,3,4,5, and 6 bonds respectively.[36,64,69,70] Hydroxyl substituents on C(1) to C(4) of 4a-methyl-*trans*-decahydronaphthalene (34b) exert an α deshielding effect of ca. 40 p.p.m. and a β deshielding effect of 3-9 p.p.m. Carbons γ to the substituent experience an upfield shift of up to 8 p.p.m., usually of lower magnitude than the β shift. In some cases for γ-carbons at a ring junction a small downfield shift is observed. The more remote δ,ε and ξ shifts were all less than 3.4 p.p.m.[36] In a study of the c.m.r. spectra of a series of 6β-substituted-3β-acetoxy-5α-cholestan-5-ols a consistent downfield γ and δ shift

parallel with the size of the substituent (F, OMe, H, OAc, OH, Cl, CH_3, Br and I) was observed.[70]

In this study spectra were recorded for a series of 4a-methyl-*trans*-decahydronaphthalenes bearing hydroxy and acetoxy substituents on C(1) and C(8a), and the changes in chemical shift with substituents are shown in tables VI and VII. The spectrum of t-4a-methyl-*trans*-decahydronaphthalen-r-1-ol (34c) recorded for a pure sample confirms the assignments made by Grover and Stothers[36] from a mixture of t-4a-methyl-*trans*-decahydronaphthalen-r-1-ol (34c) and c-4a-methyl-*cis*-decahydronaphthalen-r-1-ol (33b). The introduction of an hydroxyl function to the ring junction (C(8a)) causes an α shift of 29 p.p.m. which is considerably less than the α effect of an hydroxy substituent on C(1)-C(4). However an acetoxy substituent at C(8a) exerts an α effect comparable with an acetate or alcohol on C(1) - C(4). The β,γ, and δ effects of a C(8a) hydroxyl function are comparable to the effects reported for C(1) - C(4) hydroxyl functions in 4a-methyl-*trans*-decahydronaphthalene[36]. It is noted that the chemical shifts recorded for 4a-methyl-*trans*-decahydronaphthalene-r-1,t-4a-diol (28c) differ from values calculated by adding the substituent effects observed c-4a-methyl-*trans*-decahydronaphthalen-r-1-ol (34d) and 8a-methyl-*trans*-decahydronaphthalen-4a-ol (28a) by up to 4 p.p.m. This indicates that care should be taken calculating c.m.r. peak positions for polysubstituted compounds.

TABLE VI

C.m.r. Chemical Shifts[a] of 4a-methyl-*trans*-decahydronaphthalenols and acetates

Compound	34b	28a	34d	34c	28c	34e	34f	29b
Carbon								
1	29.3_6[b]	34.2_7	71.8[c]	70.4_8	75.3_2	73.6_4	76.2_5	69.9_1
2	27.4_2	20.7_0	34.1	36.6_2	29.2_5	32.8_2	26.2_6	24.4_1
3	22.2_4	20.9_9	16.9	20.3_1	16.4_9	20.1_3	16.9_2	16.4_0
4	42.4_4	34.9_4	43.7	41.2_0	36.9_0	40.9_3	36.2_6	36.8_0
5	42.4_4	34.9_4	41.7	41.8_9	34.9_5	41.8_1	34.5_1	34.4_7
6	22.4_4	20.9_9	21.9	21.6_5	20.4_2	21.5_0	20.5_8	20.5_0
7	27.4_2	20.7_0	27.2	26.6_4	20.8_8	26.4_7	20.7_6	21.3_8
8	29.3_6	34.2_7	26.0	22.9_4	30.8_0	23.1_6	30.7_7	26.2_6
4a	46.1_7	75.5_5	48.5	52.5_3	73.9_1	49.4_6	73.2_9	86.3_2
8a	34.7_8	36.7_8	33.7	34.8_6	36.2_7	35.1_7	36.4_1	37.4_9
CH_3	15.7_5	20.3_1	19.1	16.8_9	20.4_2	16.7_2	20.3_1	20.8_0

[a] Relative to TMS

[b] Reference 52

[c] Reference 36

Table VII

Substituent Effects[a] of Hydroxy and Acetoxy Groups in 4a-Methyl-*trans*-decahydronaphthalene.

α	β	γ	δ	ε	compound
$+29.3_8$ C(9)	$+4.9_1$ C(1),C(8); $+1.9_4$ C(9)	-6.7_0 C(2),C(7); -7.5_0 C(4),C(5); $+4.5_6$ CH_3	-1.2_5 C(3), C(6)		(28a)
$+42.4_4$ C(1)	$+6.6_8$ C(2); $+2.3_3$ C(9)	-5.3_4 C(3); -3.3_6 C(8); -1.0_8 C(10)	$+1.2_6$ C(4); -0.1_0 C(7); -0.7_4 C(5); $+3.3_5$ CH_3	-0.5_4 C(6)	(34d)
$+41.1_2$ C(1)	$+9.2_0$ C(2); $+6.3_6$ C(9)	-1.9_3 C(3); -6.4_2 C(8); $+0.0_8$ C(10)	-1.2_4 C(4); -0.7_8 C(7); -0.5_5 C(5); $+1.1_4$ CH_3	-0.7_9 C(6)	(34c)
$+44.2_8$ C(1)	$+5.4_0$ C(2); $+3.4_5$ C(9)	-2.1_1 C(3); -6.2_0 C(8); $+0.3_9$ C(10)	-1.5_1 C(4); -0.9_5 C(7); -0.6_3 C(5); $+0.9_7$ CH_3	-0.9_4 C(6)	(34e)

[a] Values represent $\delta C^{ROR'} - \delta C^{RH}$ (R' = H or Ac).

Dehydration of 8a-methyl-decahydronaphthalen-4a-ols

If the dehydration reactions of 8a-methyl-decahydronaphthalen-4a-ols induced by $SOCl_2$-pyridine and H_2SO_4-Ac_2O-AcOH were to be analogous with those of C(5) steroids, products of 1,2 elimination, methyl migration followed by elimination, and spiran formation might be expected. For 8a-methyl-*trans*- and *cis*-decahydronaphthalen-4a-ol (28a) and (27a) 1,2 elimination and methyl migration followed by 1,2 elimination give 8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalene (23a). These reaction paths therefore can not be distinguished unless the starting material is suitably labelled. The following deuterated substrates were prepared: 8a-methyl-*trans*-decahydronaphthalen-r-4a-ol-t-5-*d* (28b), 8a-methyl-*trans*-decahydronaphthalen-r-4a-ol-c-5-*d* (28g), and 8a-methyl-*cis*-decahydronaphthalen-r-4a-ol-t-5-*d* (27b) and their elimination reactions studied. Any one of these substrates might be expected to undergo elimination to give a mixture of unlabelled 8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalene (23a), 8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalene (23a) labelled with deuterium in four different positions, and possibly spiran olefins (e.g. fig. 14). In this study the compositions of the product mixtures obtained on $SOCl_2$-pyridine and H_2SO_4-Ac_2O-AcOH dehydration of the deuterium labelled 8a-methyl-*cis*- and *trans*-decahydronaphthalen-4a-ols (27b), (28b) and (28g), were determined by c.m.r., p.m.r. and mass spectroscopy. No spiran olefins were detected in the product mixtures. The presence of deuterium at

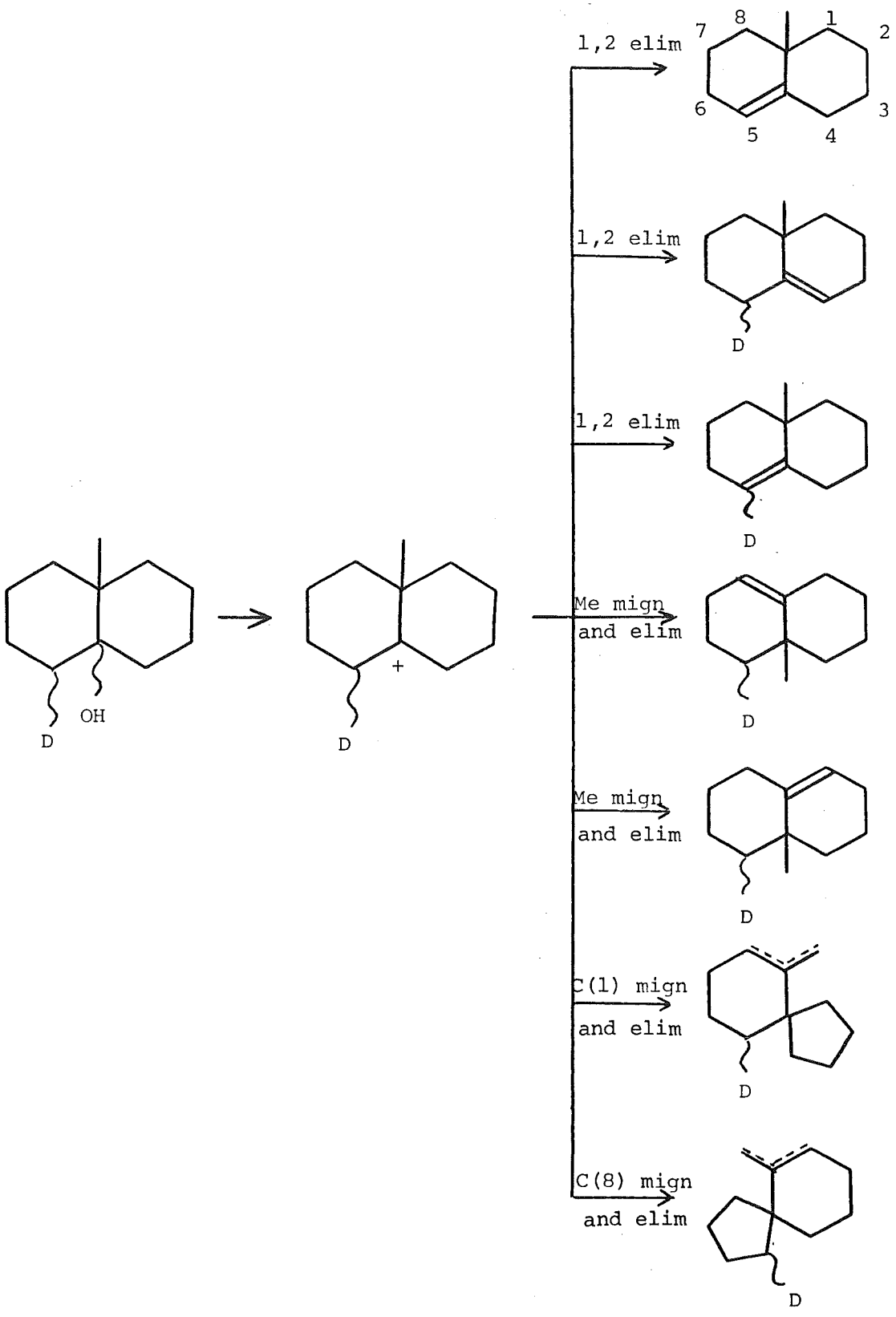

OH
D
+
D
1,2 elim
8
1
7
2
6
3
5
4
1,2 elim
D
1,2 elim
D
Me mign
and elim
D
Me mign
and elim
D
C(1) mign
and elim
D
C(8) mign
and elim
D

Figure 14.

C(4) and C(5) in 8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalene was determined from the SFOR c.m.r. spectrum. Because deuterium absorptions occur well away from the proton region of the spectrum, single frequency offset resonance decoupling of the protons does not remove deuterium - carbon couplings. Therefore in the proton decoupled c.m.r. spectrum carbons bearing a deuterium substituent appear as triplets. In addition, long range coupling of deuterium with adjacent carbons causes line broadening with a consequent reduction in peak height of the appropriate carbon signal. Because of a lengthening of the spin-lattice relaxation times caused by a deuterium substituent, the resonances of carbons bearing a deuterium substituent are often reduced in intensity. A slight change in the chemical shift of deuterated carbons was also observed. The proportion of unlabelled 8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalene (23a) to deuterated 8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalene in the product mixtures was determined by measuring the relative intensities of the peaks corresponding to the parent ions of undeuterated and deuterated 8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalene in the mass spectrum. The presence of 8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalene-1-*d* (23b) was determined by a decrease in the relative intensity of the vinyl proton signal (cf. C(8a)-methyl) compared with the p.m.r. spectrum of an undeuterated sample of 8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalene

Dehydration of 8a-methyl-*trans*-decahydronaphthalen-r-4a-ol-t-5-*d* (28b) with $SOCl_2$-pyridine gave

8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalene partially labelled with deuterium as the only isolable product. The c.m.r. spectrum of the olefin showed two resonances for C(4); a singlet at δ32.64, and a triplet centred at δ32.36 (J 0.95 p.p.m.). A decrease was observed in the peak heights of the C(3) and C(4a) resonances. All other carbon resonances had the same chemical shifts and peak heights relative to the methyl resonance as for a spectrum of authentic undeuterated 8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalene (23a). This c.m.r. spectrum is consistent with the product being a mixture of 8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalene (23a) and r-8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalene-c-4-*d* (23c). Analysis of the mass spectrum of the reaction product and in particular the relative intensity of the $\frac{m}{e}$ peaks at 152, 151 and 150 in comparison with the $\frac{m}{e}$ 151, 150 and 149 peaks of an authentic sample of undeuterated 8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalene (23a) allowed the ratio of 8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalene (23a) to r-8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalene-c-4-*d* (23c) to be determined as 7:13 (fig. 21, p.64). The kinetic isotope effect k_H/k_D for the reaction is therefore 1.88 (±0.15). Comparison of the p.m.r. integral of the olefinic proton (δ5.25) relative to the integral of the methyl protons (δ1.05) confirms the absence of deuterium on C(5).

The c.m.r. spectrum of the mixture of olefins obtained by dehydration of 8a-methyl-*cis*-decahydronaphthalen-4a-ol (27b) with thionyl chloride-pyridine showed $C(4)H_2$

as a singlet at δ32.64 p.p.m. and the C(4)HD as a triplet centred at δ32.36 p.p.m. (J 0.95 p.p.m.). A decrease in peak heights of the C(3) and C(4a) resonances was observed in the spectrum of the olefin mixture due to long range coupling wth the C(4) deuterium in the deuterated olefin. All other carbon resonances had similar chemical shifts and intensities relative to the methyl resonance as for the spectrum of 8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalene (23a). The reaction product is therefore a mixture of 8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalene (23a) and r-8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalene-t-4-*d* (23d). In the p.m.r. spectrum of the olefin mixture the vinyl: methyl resonance integral ratio was 1:3. This confirms the absence of deuterium at C(5). From a comparison of the intensity of the $\frac{m}{e}$ peaks at 152, 151 and 150 in the mass spectrum of the product mixture with $\frac{m}{e}$ peaks at 151, 150 and 149 in an authentic sample of un-deuterated 8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalene (23a) the ratio of 8a-methyl-1,2,3,4,6,7,8,8a-octahydro-naphthalene (23a) to r-8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalene-t-4-*d* (23d) was calculated as 43:57 (fig. 21, p. 63). The kinetic isotope effect k_H/k_D for the reaction is therefore 1.33 (±0.2).

The chair-chair conformation of 8a-methyl-*trans*-decahydronaphthalen-r-4a-ol-t-5-*d* (28b) is the lowest energy conformation. In this conformation (fig. 15) the C(5) deuterium is anticoplanar with the C(4a) leaving group. The observation that loss of deuterium from C(5) occurs in the reaction of 8a-methyl-*trans*-decahydronaphthalen-

r-4a-ol-t-5-*d* (28b) with thionyl chloride-pyridine and that no detectable quantities of 8a-methyl-1,2,3,4, 6,7,8,8a-octahydronaphthalen-5-*d* (23b) are present in the product mixture demonstrates that elimination of hydrogen from C(5) occurs *anti*- to the C(4a)-hydroxyl function. The symmetry of 8a-methyl-*trans*-decahydronaphthalen-r-4a-ol-t-5-*d* (28b) about the C(4a)-C(8a) bond implies equivalence of C(5) and C(4) and therefore elimination of hydrogen from C(4) must also be *anti*- to the C(4a) leaving group (fig. 15). The anticoplanar stereo-specificity of elimination observed for this reaction is consistent with a mechanism in which proton abstraction occurs in concert with departure of the leaving group. Kinetic isotope effects for bimolecular elimination processes are maximal if the transition state for the elimination is symmetrical, and deuterium isotope effects as high as 8 have been reported for these reactions.[71] The observed k_H/k_D of 1.88 for the elimination of water from 8a-methyl-*trans*-decahydronaphthalen-r-4a-ol-t-5-*d* (28b) in thionyl chloride-pyridine implies that the transition state for this reaction is unsymmetrical. Since the sulphonyl chloride ester is regarded as a good leaving group[25] it is likely that C-O bond cleavage is more advanced in the transition state than C-H bond cleavage.

At ambient temperatures the degenerate chair-chair conformations (37) and (38) of 8a-methyl-*cis*-decahydronaphthalen-r-4a-ol-t-5-*d* are undergoing rapid interchange (fig. 16). In conformation (37) the C(5) deuterium is diaxial and

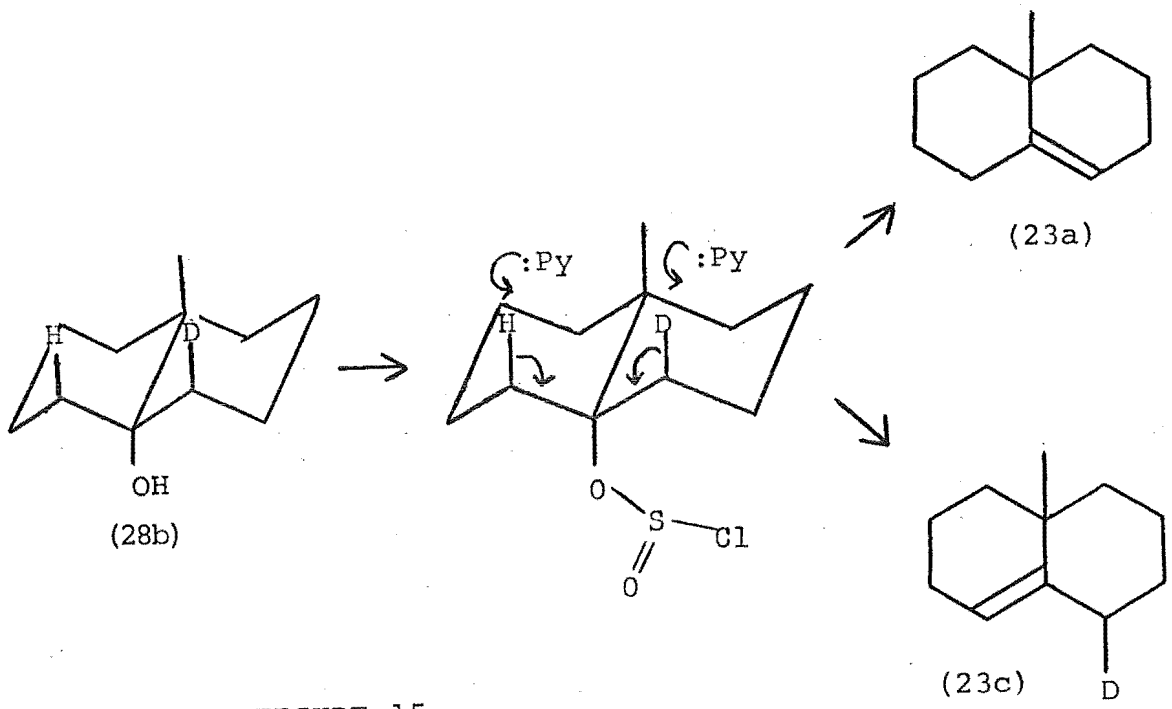


FIGURE 15.

anticoplanar with the C(4a) leaving group, but this is not the case for C(4) hydrogens. In conformation (38) a C(4) hydrogen is anticoplanar to the leaving group but the C(5) deuterium is not. The observed products of reaction of 8a-methyl-*cis*-decahydronaphthalen-r-4a-ol-t-5-*d* (27b) in thionyl chloride - pyridine, namely 8a-methyl-1,2,3,4, 6,7,8,8a-octahydronaphthalene (23a) and r-8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalene-t-4-*d* (23d) are considered, by analogy with the stereochemical course of the dehydration of 8a-methyl-*trans*-decahydronaphthalen-r-4a-ol-t-5-*d* (28b) in thionyl chloride-pyridine, to occur *via* anticoplanar elimination of the C(5) deuterium from conformation (37), and anticoplanar elimination of the axial C(4) proton from conformation (38) of 8a-methyl-

cis-decahydronaphthalen-r-4a-ol-t-5-*d* (27b) respectively (fig. 16).

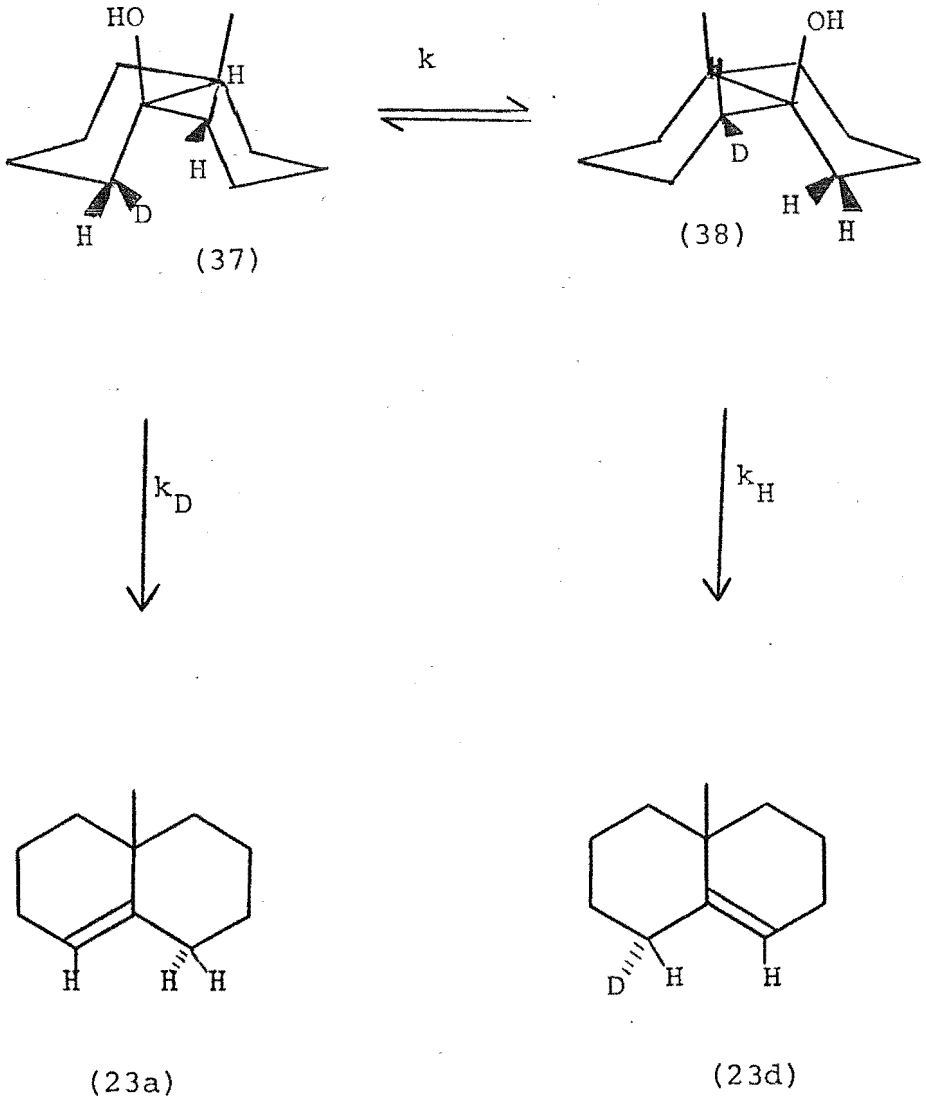


Figure 16.

The ratio (1.3 ± 0.2) of olefin (23d) to olefin (23a) formed in thionyl chloride-pyridine from 8a-methyl-*cis*-decahydronaphthalen-r-4a-ol-t-5-*d* (27b) is lower than the ratio (1.88 ± 0.15) of olefin (23c) to olefin (23a) observed for similar dehydration of 8a-methyl-*trans*-decahydronaphthalen-r-4a-ol-t-5-*d* (28b). The C(5)

and C(4) protons *anti* to the hydroxyl group of the *cis*-alcohol (27b) are in a more sterically crowded environment than the C(5) and C(4) protons *anti* to the hydroxyl group in the *trans*- alcohol (28b). The axial protons on C(3) or C(5) in conformations (37) and (38) respectively would be expected to hinder the approach of base to the C(5) and C(4) protons. Therefore it is likely that the transition state will be even less symmetric for thionyl chloride dehydration 8a-methyl-*cis*-decahydronaphthalen-r-4a-ol-t-5-*d* (27b) than for 8a-methyl-*trans*-decahydronaphthalen-r-4a-ol-t-5-*d* (28b). The C-O bond cleavage is therefore expected to be further advanced in the transition state for dehydration of 8a-methyl-*cis*-decahydronaphthalen-r-4a-ol-t-5-*d* (27b). Since the conformations (37) and (38) of 8a-methyl-*cis*-decahydronaphthalen-r-4a-ol-t-5-*d* (27b) are degenerate, if the rate of conformational change between these conformers is very much slower than the rate of elimination ($k \ll k_{H(D)}$, fig. 16), the ratio of hydrogen loss to deuterium loss would tend to 1:1. If however $k \gg k_{H(D)}$, the ratio of olefin (23d) to olefin (23a) would give a measure of the isotope effect k_H/k_D for the reaction. Since the observed k_H/k_D is significantly greater than 1.0 the conformational equilibrium must be at least competitive with elimination.

Dehydration of 8a-methyl-*trans*-decahydronaphthalen-r-4a-ol-t-5-*d* (28b) in H_2SO_4-Ac_2O-AcOH was rapid and no starting material could be detected in the product mixture after 20 seconds. The c.m.r. spectrum (table IX, p. 61)

showed C(4) as a triplet centred at δ32.4 (H0.9 p.p.m.) superimposed on a singlet δ32.6 and C(5) as a triplet centred at δ119.0 (J 1.17 p.p.m.) superimposed on a singlet of δ119.3. The adjacent C(3) and C(6) carbons exhibited long range coupling with deuterium and were reduced in peak height compared with an authentic sample of 8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalene (23a). The remaining carbon signals were the same as for 8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalene. The mass spectrum of the product olefin mixture indicated that no measurable loss i.e. < 5% of the deuterium label had occurred. In the p.m.r. spectrum of the olefin mixture the integrals of the vinyl proton (δ5.25) and the methyl protons (δ1.05) were in the ratio 1:6. With the mass spectral and c.m.r. data this shows that the product is a 1:1 mixture of 8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalene-5-*d* (23b) and r-8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalene-c-4-*d* (23c).

In the dehydration of 8a-methyl-*trans*-decahydronaphthalen-r-4a-ol-t-5-*d* (28b) in H_2SO_4-Ac_2O-AcOH to give olefins (23b) and (23c) the proton at C(5) *syn*- to the leaving group is lost. In the absence of an extremely large kinetic isotope effect the symmetry of 8a-methyl-*trans*-decahydronaphthalen-r-4a-ol-t-5-*d* (28b) requires that the C(4)H *syn*- to the leaving group must also be lost, in the formation of r-8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalene-c-4-*d* (23c). By analogy with the steroid studies mentioned earlier it can be assumed that these reactions proceed by way of a carbonium ion intermediate.

Cleavage of the C(4a)-oxygen bond in the dehydration of 8a-methyl-*trans*-decahydronaphthalen-r-4a-ol-t-5-*d* (28b) would give a C(4a) carbonium ion which could undergo conformational changes in competition with further reaction (fig. 17). In conformation (44) the C(5)-D and a C(4)-H are aligned with the vacant C(4a)- p-orbital. However it is notable that no deuterium

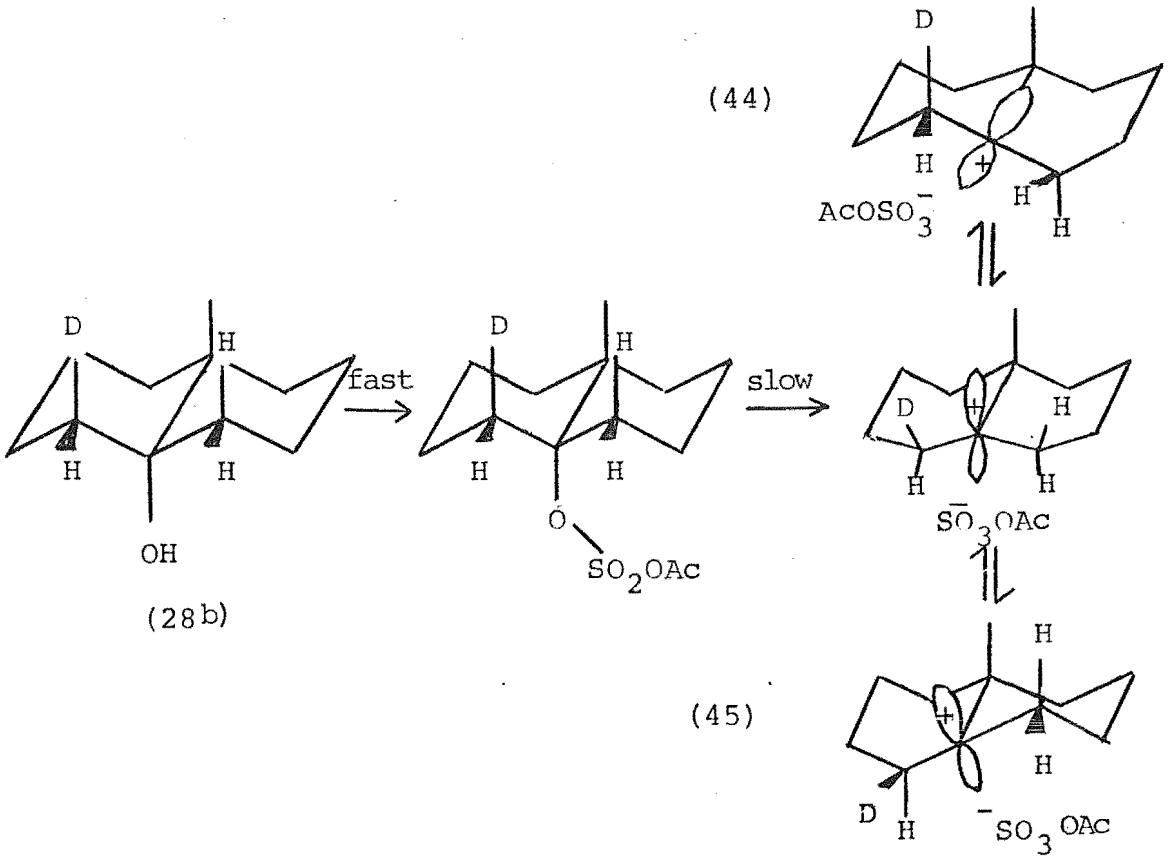


Figure 17.

is lost in the reaction. This can be accounted for if the acetyl sulphonate anion is retained on the underside of the molecule and acts as the base for proton removal. The reaction products r-8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalene-c-4-*d* (23c) and 8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalene-5-*d* (23b) are therefore formed by abstraction of the C(4)H *syn* to the oxy-anion in conformer (44) (fig. 17), and the C(5)H *syn* to the oxy anion in conformer (45) respectively. In contrast with many steroid substrates no products of methyl migration are observed.

Bathurst *et al.* have reported that the elimination reaction of 4α-acetoxy-5α-cholestan-5-ol-6β-*d* (46) in H_2SO_4-Ac_2O-HOAc occurs with retention of the deuterium label to give 4α- and 4β-acetoxycholest-5-ene-6-*d*.[11] The stereospecificity of this elimination was originally discussed in terms of the relative stabilities of conformers (10) and (12) of the C(5) carbonium ion intermediate (fig. 18). However in view of the results obtained in this study it seems more likely that the reaction proceeds via the intermediacy of a tight ion pair, where the anionic moiety is retained on the α-face of the molecule and acts as base for removal of the only adjacent *syn*-hydrogen.

To obtain a value for the kinetic isotope effect for proton loss for dehydration of 8a-methyl-*trans*-decahydronaphthalen-4a-ol (28a) in H_2SO_4-Ac_2O-HOAc a sample of 8a-methyl-*trans*-decahydronaphthalen-r-4-ol-c-5-*d* (28g) was prepared and its dehydration reaction studied. Dehydration of 8a-methyl-*trans*-decahydronaphthalen-r-4a-ol-c-5-*d* (28g)

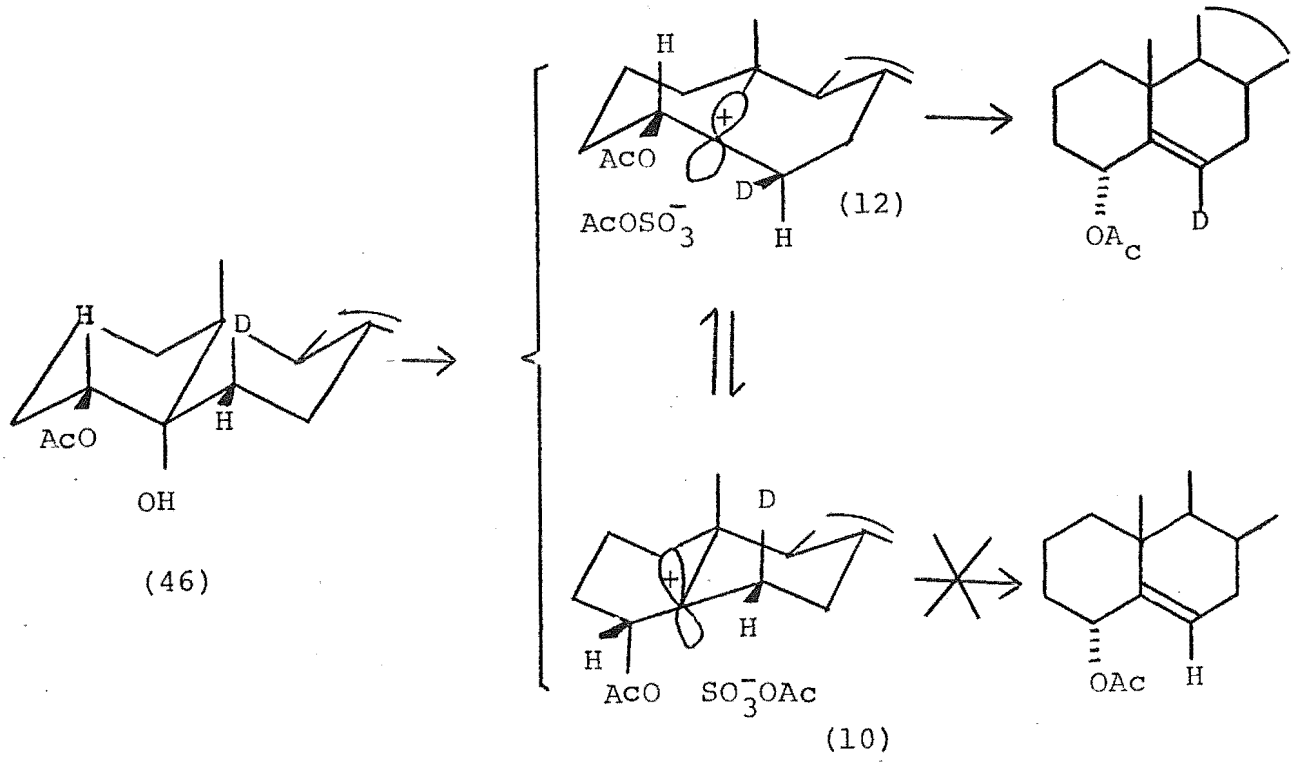


Figure 18.

which was contaminated with unlabelled 8a-methyl-*trans*-decahydronaphthalen-4a-ol (28a, 5%) and 5,6-dideuterated 8a-methyl-*trans*-decahydronaphthalene-4a-ol (47, 11%) gave a mixture of undeuterated, monodeuterated and dideuterated 8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalene which contained no starting alcohol. The p.m.r. spectrum of the product mixture showed the integrals of the vinyl and methyl signals to be in the ratio 1:3 which demonstrates that deuterium has been lost from C(5) in the formation of 8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalene (23a). From an analysis of the intensity of the mass spectral peaks at $\frac{m}{e}$ 152, 151 and 150, and compensating for the presence of undeuterated and dideuterated alcohol in the starting

alcohol, 8a-methyl-*trans*-decahydronaphthalen-r-4a-ol-c-5-*d* (28g) was found to give 8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalene (23a) and r-8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalene-t-4-*d* (23d) in the ratio 1:2.2 (±0.4).

The preference for loss of a proton demonstrates that conformational interchange of the degenerate C(4a) carbonium ion conformers is at least competitive with proton (deuteron) loss (fig. 19). If conformational interchange were not competitive with elimination no kinetic isotope effect would be observed.

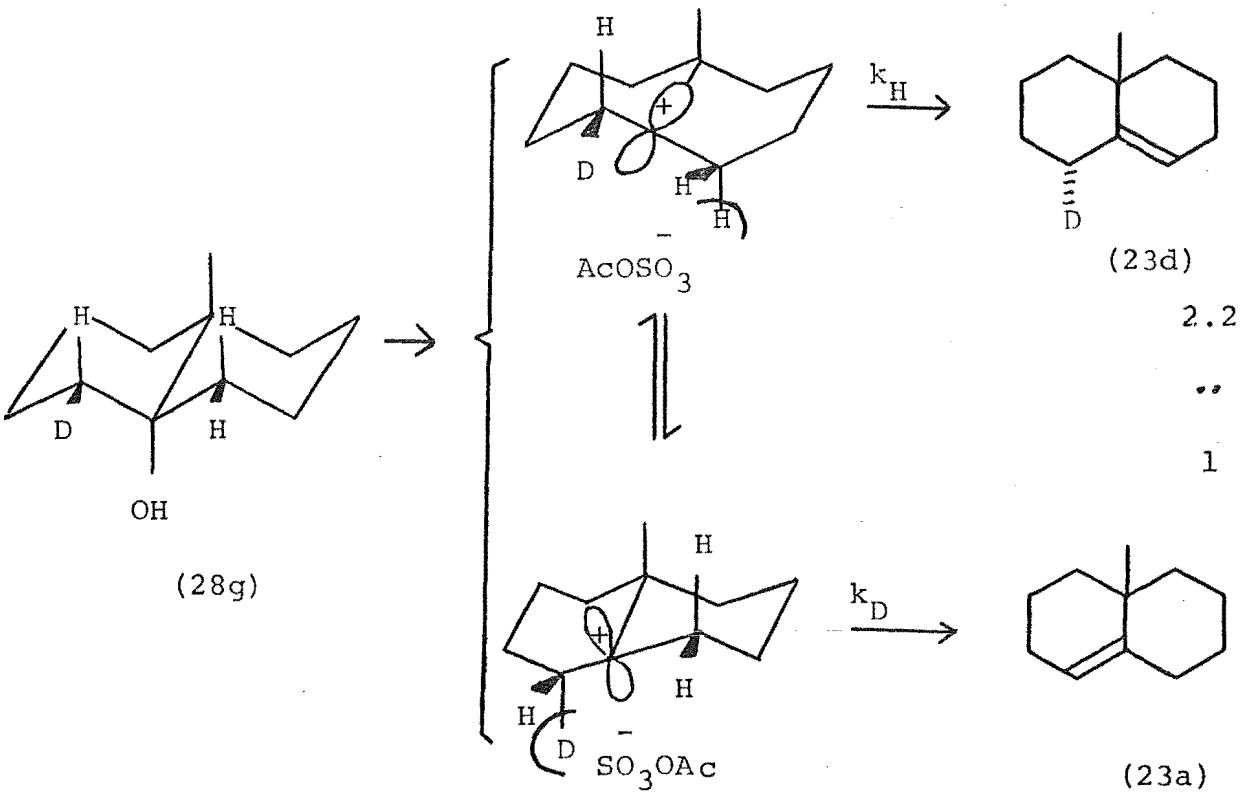


Figure 19.

The only product which could be isolated from reaction of 8a-methyl-*cis*-decahydronaphthalen-r-4a-ol-t-5-*d* (27b) with H_2SO_4-Ac_2O-AcOH for 20 seconds was deuterated 8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalene. The c.m.r. spectrum of the product mixture showed C(4) as a triplet centred at δ32.4 (J 0.9 p.p.m.) superimposed on a singlet at δ32.6 and C(5) as a triplet centred at δ119.0 (J 1.17 p.p.m.) superimposed on a singlet at δ119.3. Deuterium is therefore present at both C(4) and C(5). The resonances for C(3) and C(6) are reduced in intensity by long range coupling with deuterium. The mass spectrum showed that no measureable loss (i.e. < 5%) of deuterium had taken place. The product is therefore a mixture of 8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalene-5-*d* (23b) and r-8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalene-t-4-*d* (23d). From the integrals in the p.m.r. spectrum of the vinyl proton at δ5.25 and the methyl protons at δ1.05 the deuterium content at C(5) was determined as 48 (±5)%. It follows that C(4) contains the remaining deuterium label.

The retention of the C(5) deuterium label in the formation of 8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalene-5-*d* (23b) demonstrates that in this reaction loss of the C(4) and C(5) protons *syn* to the leaving group occurs. Superficially at least elimination from 8a-methyl-*cis*-decahydronaphthalen-4a-ol (27a) and 8a-methyl-*trans*-decahydronaphthalen-4a-ol (28a) would proceed *via* the same C(4a)-carbonium ion intermediate. The stereospecific loss of hydrogen *syn*- to the leaving group

for both these compounds is consistent with the departing oxy-anion acting as base in the removal of the adjacent proton. The regiospecifity observed in the elimination from 8a-methyl-*cis*-decahydronaphthalen-r-4a-ol-t-5-*d* (27b) and 8a-methyl-*trans*-decahydronaphthalen-r-4a-ol-t-5-*d* (28b) demonstrates that anion transfer to the opposite face of the carbonium ion intermediate does not compete with proton loss. It is significant that the anion is retained on the more hindered face of the C(4a)- carbonium ion formed from 8a-methyl-*cis*-decahydronaphthalen-r-4a-ol-t-5-*d* (27b) despite steric compression with the C(8a) methyl (fig. 20).

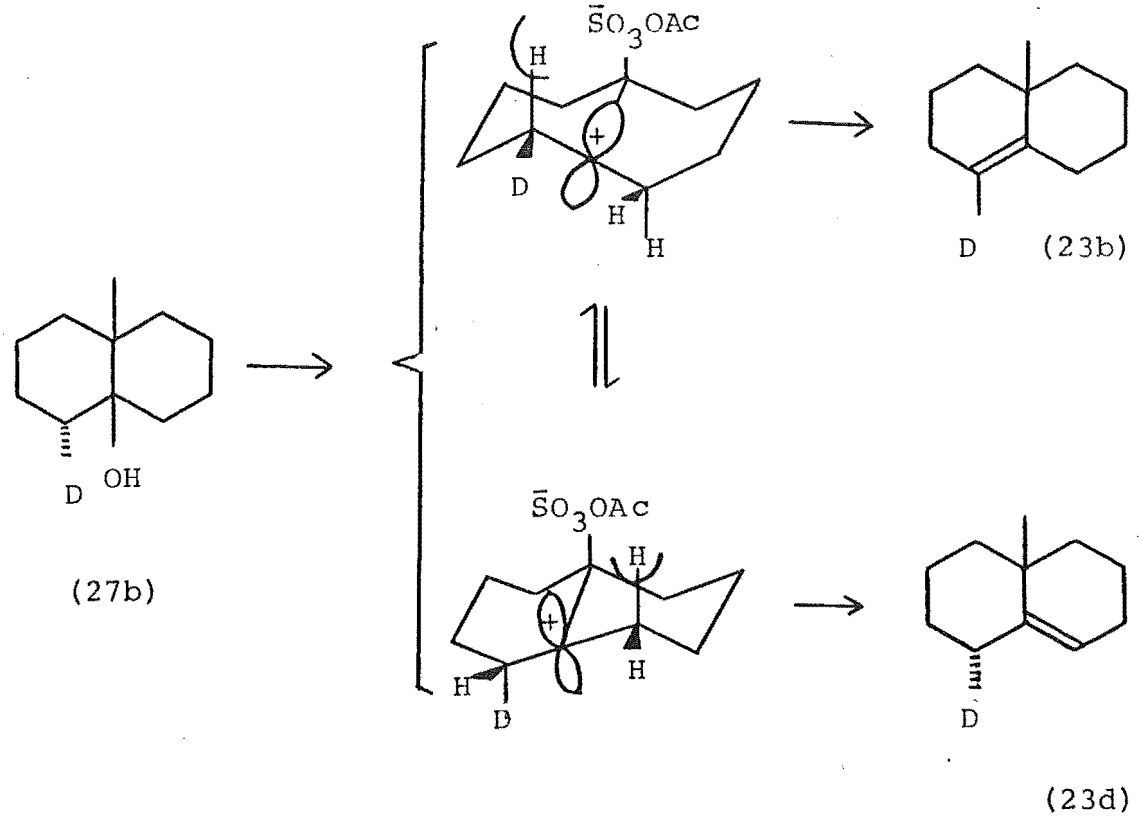


Figure 20.

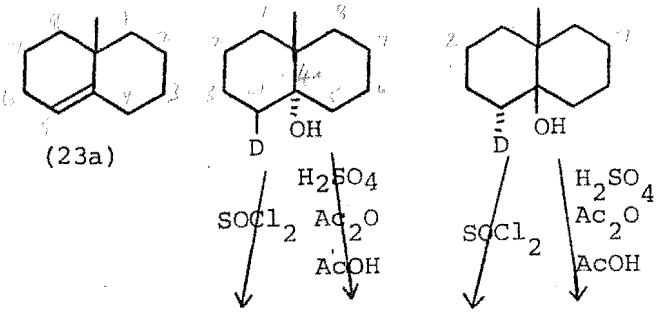
The chemical shifts and peak heights relative to the methyl resonance of the c.m.r. single frequency offset resonance decoupled spectra of the product mixtures obtained from dehydration of 8a-methyl-*trans*-decahydronaphthalen-r-4a-ol-t-5-*d* (28b) and 8a-methyl-*trans*-decahydronaphthalen-r-4a-ol-t-5-*d* (27b) in $SOCl_2$-pyridine and H_2SO_4-Ac_2O-AcOH are shown in Table IX. An authentic sample of 8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalene (23a) was prepared by lithium-ammonia reduction of 4a-methyl-1,2,3,4,6,7,8,8a-octahydronaphth-2-yl acetate (48a).

The height of a C-13 resonance is a function of both relaxation time and long range coupling effects. For the undeuterated olefin the bridgehead carbon resonances are more than 50%, and the C(5) resonance 13%, smaller than the methyl and methylene resonances. This is consistent with the known increase in relaxation times as hydrogen is replaced by alkyl substituents. This effect canbe minimised by recording the spectrum with a long delay between pulses to allow relaxation to occur. Such precautions are only practicable when working with large samples. Fortunately in this study this was not found necessary since a reference sample of undeuterated olefin was available for comparison purposes.

In the c.m.r. spectra of the deuterated olefins obtained from dehydration in H_2SO_4-Ac_2O-AcOH and $SOCl_2$-pyridine of the deuterated 8a-methyldecahydronaphthalen-4a-ols (27b) and (28b) the C(3) signal was reduced in

TABLE IX

C-13 n.m.r. Chemical Shifts and Peak heights of Dehydration products



Carbon	δ^a	Ht^b	Ht^b	Ht^b	Ht^b	Ht^b
1	42.2	1.1	1.0	0.98	0.93	1.0
2	22.5	0.99	1.1	1.0	0.91	0.91
3	28.3	1.1	0.57	0.70	0.70	0.60
4	32.3	0.93	0.42[c]	0.36[c]	0.47[c]	0.33[c]
5	119.3	0.87	0.65	0.40[d]	0.53	0.35[d]
6	26.0	1.1	1.1	0.65	0.99	0.67
7	19.1	0.98	0.97	0.88	1.1	0.91
8	40.1	0.94	1.0	1.0	0.96	0.95
4a	143.4	0.30	0.17	0.22	0.46	0.12
8a	34.8	0.44	0.28	0.32	0.43	0.17
CH_3	24.3	1.0	1.0	1.0	1.0	1.0

a, Relative to TMS. b, Relative to $\underline{CH}_3$ = 1.

c, Triplet δ32.4, J 0.95 p.p.m. superimposed on singlet measured.

d, Triplet δ119.0, J 1.2 p.p.m. superimposed on singlet measured.

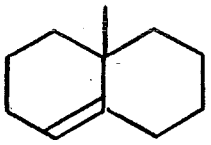
intensity *c.f.* undeuterated 8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalene (23a). For the spectrum of the olefin mixture obtained from the reaction of 8a-methyl-*trans*-decahydronaphthalen-r-4a-ol-t-5-*d* (28b) with H_2SO_4-Ac_2O-AcOH it was possible to resolve the C(3) signal into two peaks separated by 0.08 p.p.m. For product mixtures obtained from the H_2SO_4-Ac_2O-AcOH dehydration of alcohols (27b) and (28b), which contain 8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalene-5-*d*, the C(6) peak height was reduced in intensity by about 25%, and on scale expansion this peak could be resolved into a singlet and triplet (J 0.11 p.p.m.). In the products of the $SOCl_2$-pyridine dehydration of 8a-methyl-*trans*-decahydronaphthalen-r-4a-ol-t-5-*d* (28b) and 8a-methyl-*cis*-decahydronaphthalen-r-4a-ol-t-5-*d* (27b) no deuterium is present at C(5). Long range coupling of C(5) with the C(4) deuterium was observed by a loss in height of the C(5) resonance relative to 8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalene (23a) (Table IX). This reduction in peak height was not due to the presence of deuterium at C(5) since no triplet at δ119.0 could be observed and the C(6) resonance was of normal intensity.

It was possible to obtain an estimate of the extent of the deuteration at C(4) by comparing the integral of the singlet with the sum of the integrals for the triplet peaks. As deuterated and undeuterated carbons have different relaxation times and the singlet and

triplet peaks are close together, and c.m.r. integrals are less reliable than the integrals obtained from the p.m.r. spectra. The uncertainty in the c.m.r. integrals could be in excess of 20%. Values for the percentage of deuterium at C(4) of 40(±20)% and 42(±20)% were obtained for the H_2SO_4-Ac_2O-AcOH dehydration products of 8a-methyl-*trans*-decahydronaphthalen-r-4a-ol-t-5-*d* (28b) and 8a-methyl-*cis*-decahydronaphthalen-r-4a-ol-t-5-*d* (27b) respectively. This compares with values of 50(±5)% obtained from the more accurate p.m.r. integrals. Therefore, while c.m.r. spectroscopy was used to determine the location of deuterium the extent of deuteration was calculated from p.m.r. and mass spectra.

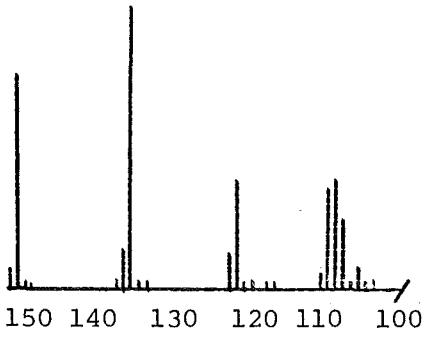
It is interesting to note that the loss of H_2O in the mass spectrometer from deuterated 8a-methyldecahydronaphthalen-4a-ols (27b) (28b) and (28g) is regiospecific. In the mass spectra of 8a-methyl-*cis*-decahydronaphthalen-r-4a-ol-t-5-*d* (27b) and 8a-methyl-*trans*-decahydronaphthalen-r-4a-ol-t-5-*d* (28b) loss of water occurs with retention of deuterium, as shown by the presence of a peak at $\frac{m}{e}$ 151 ($M^+ - H_2O$) and absence of a significant peak at $\frac{M}{e}$ 150 ($M^+ - HDO$). In contrast the mass spectrum of 8a-methyl-*trans*-decahydronaphthalen-r-4a-ol-c-5-*d* (28g) contains peaks due to both loss of H_2O and loss of HDO from the parent ion, from which it may be concluded that loss of water occurs regiospecifically by loss of a proton *syn* to the hydroxyl function. From the relative

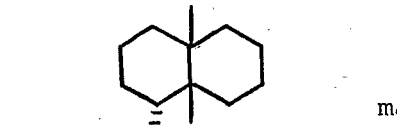
Figure 21. Mass spectra of products of dehydration of 8a-methyldecahydronaphthalen-4a-ols.



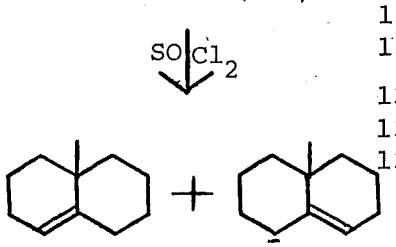
(23a)

mass	relative intensity[a]
151	12.4
150	100
149	2.1
136	12.9
135	100
134	1.0



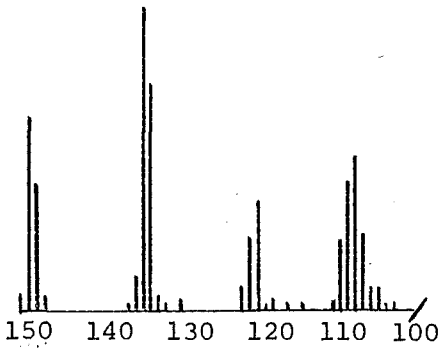


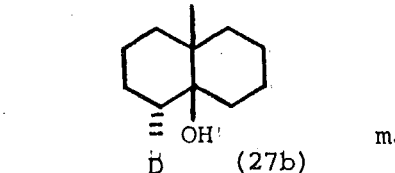
(27b)



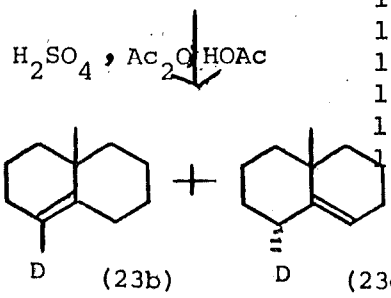
(23a) (23d)

mass	relative intensity[a]
152	14.0
151	100
150	71.3
137	11.5
136	100
135	74.5



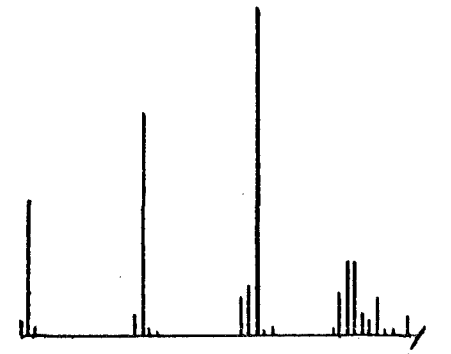


(27b)

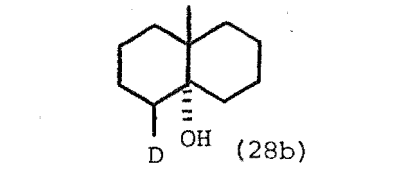


(23b) (23d)

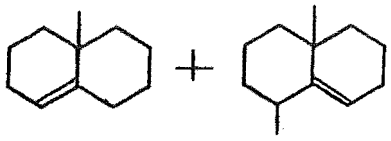
mass	relative intensity[a]
152	13.2
151	100
150	6.0
137	11.9
136	100
135	3.8



[a] = peak height relative to largest peak in group

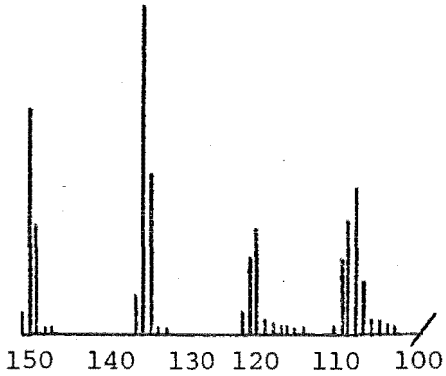


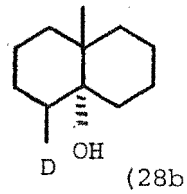
(28b)



(23a) D (23c)

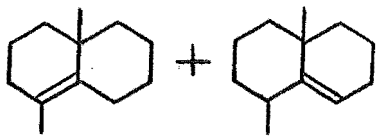
mass	relative intensity
152	12.1
151	100
150	51.7
137	10.8
136	100
135	50.0





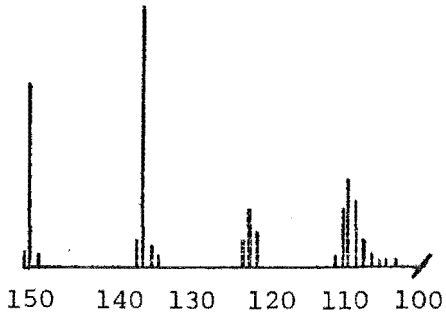
(28b)

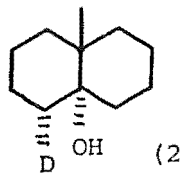
H_2SO_4, Ac_2O, HOAc



D (23b) D (23c)

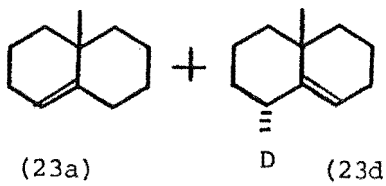
mass	relative intensity
152	13.0
151	100
150	4.7
137	13.5
136	100
135	5.4





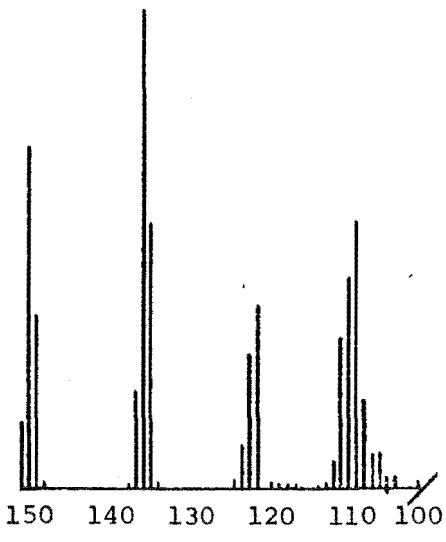
(28g)

H_2SO_4, Ac_2O, HOAc



(23a) D (23d)

mass	relative intensity
152	24.0
151	100
150	52.0
137	23.0
136	100
135	55.7



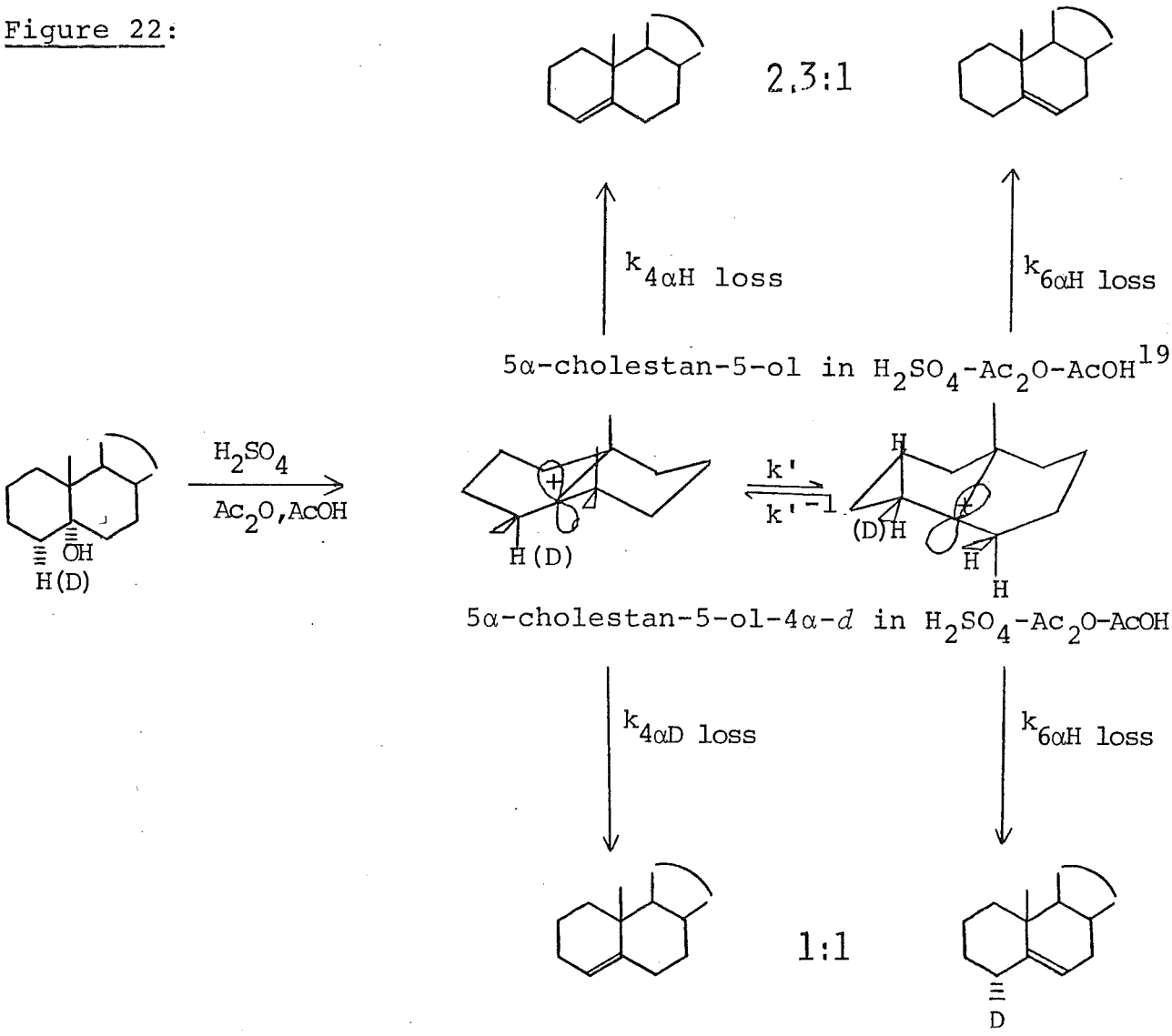
intensities of the peaks at $\frac{m}{e}$ 150 and 151, and at $\frac{m}{e}$ 135 and 136 an approximate value for the kinetic isotope effect for this process of k_H/k_D = ca. 1.6 was determined.

In order to determine the generality of the results obtained for the dehydration of 8a-methyldecahydronaphthalen-4a-ols (27b), (28b) and (28g) in H_2SO_4-Ac_2O-AcOH, the reaction of 5α-cholestan-5-ol (3e) labelled at the 4α-position with deuterium was investigated. Dehydration of 5α-cholestan-5-ol (3e) in H_2SO_4-Ac_2O-AcOH has been previously shown to give a mixture (7:3) of cholest-4-ene (14a) and cholest-5-ene[19] (7c).

The 5α-cholestan-5-ol-4α-*d* (3f) was prepared by reduction with lithium aluminium hydride of 4,5-epoxy-5α-cholestane-4β-*d* (49) prepared by Blackett.[73] Dehydration with H_2SO_4-Ac_2O-HOAc afforded a mixture of cholest-4-ene (14a) and cholest-5-ene-4α-*d* (7d). Integration of the vinyl protons in the p.m.r. spectrum showed there to be no measurable deuterium label (< 5%) on the vinyl carbons. From a comparison of the $[\alpha]_d$ of the product mixture (+ 6.4°) with the values reported[19,74] for cholest-4-ene (+ 66°) and cholest-5-ene (-56°) the product composition of cholest-4-ene and cholest-5-ene can be determined as 1:1. Mass spectral analysis shows that 45 ± 5% of the deuterium was lost during dehydration. This implies that cholest-4-ene is formed by specific loss of the 4α-deuterium and is consistent with the results obtained for the 8a-methyldecahydronaphthalen-4a-ols. Comparison of the product ratios obtained in the dehydration of 5α-cholestan-5-ol with those obtained for 5α-cholestan-

5-ol-4α-*d* (2.3:1 *cf.* 1:1) indicates a primary kinetic isotope effect of k_H/k_D = *ca.* 2.3 (fig 22). This value, within the limits of the experimental method, is remarkably comparable with that found for 8a-methyl-*trans*-decahydronaphthalene (k_H/k_D = 2.2).

Figure 22:



If k' and k'^{-1} >> $k_{4\alpha H(D)}$ loss and $k_{6\alpha H}$ loss

then $\frac{k_{4\alpha H}}{k_{6\alpha H}} = \frac{2.3}{1}$,

If k' ≈ k, then $\frac{k_{4\alpha H}}{k_{6\alpha H}}$ has a minimum value of 2.3.

Reaction of t-8a-hydroxy-4a-methyl-*trans*-decahydronaphth-r-1-yl acetate (28h) with H_2SO_4-Ac_2O-AcOH gave an inseperable mixture of c-8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphth-r-1-yl acetate (24b, 50%); c-8a-methyl-1,2,3,5,6,7,8,8a-octahydronaphth-r-1-yl acetate (50a, 33%); 4a-methyl-2,3,4,4a,5,6,7,8-octahydronaphth-1-yl acetate (23e) and 4a-methyl-*trans*-1-decahydronaphthalen-1-one (32a), the last two compounds constituting 17% of the product mixture. The identity of c-8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphth-r-1-yl acetate (24b), 4a-methyl-2,3,4,4a,5,6,7,8-octahydronaphth-1-yl acetate (23e) and 4a-methyl-*trans*-decahydronaphthalen-1-one (32a) follow from independent synthesis, c-8a-methyl-1,2,3,5,6,7,8,8a-octahydronaphth-r-1-yl acetate (50a) was identified from the spectral characteristics of its ketone derivative. The product mixture on reaction with L.A.H. gave c-4a-methyl-*trans*-decahydronaphthalen-r-1-ol (34d), a known compound[36] in an amount equivalent to the enol acetate (23e) and ketone (34a) products. The formation of ketone is thought to arise by hydrolysis of the enol acetate (23e) in the isolation of the reaction mixture. Such a process is not unprecedented in Westphalen dehydration of steroids.[11,12] The L.A.H. reduction of the product mixture also gave c-8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalen-r-1-ol (24a) and c-8a-methyl-1,2,3,5,6,7,8,8a-octahydro-naphthalen-r-1-ol (50b), which were seperable by g.l.c. from c-4a-methyl-*trans*-decahydronaphthalen-r-1-ol (34d). Oxidation of the mixture of c-8a-methyl-1,2,3,4,6,7,8,8a-

octahydronaphthalen-r-1-ol (24a) and c-8a-methyl-1,2,3,5,6,7,8,8a-octahydronaphthalen-r-1-ol (50b) with Jones reagent gave 8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalen-1-one (51) and 8a-methyl-1,2,3,5,6,7,8,8a-octahydronaphthalen-1-one (52) which were separated by preparative g.l.c. Ketone (51) and acetate (24b) were independently synthesized from c-8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalen-r-1-ol (24a) prepared from 8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalene-1,6-dione (22) by the method of Marshall and Bundy,[30] and found to have identical spectral and chromatographic characteristics to the major product from the dehydration reaction and its derivatives. The keto-olefins (51) and (52) showed ultra violet absorptions at *ca.* 300 nm (ε 68 and ε 130 respectively) characteristic of a β,γ- unsaturated ketone chromophore. The absorption for the 4,4a-olefin (52) was twice as intense as for the 4a,5-olefin (51), which indicates a different relative orientation of the olefinic and carbonyl moieties for each compound.

Authentic samples of 4a-methyl-2,3,4,4a,5,6,7,8-octahydronaphth-1-yl acetate (23e) and 4a-methyl-*trans*-decahydronaphthalen-1-one (32a) were prepared from a mixture of c-4a-methyl-*cis*-decahydronaphthalen-r-1-ol (33b) and t-4a-methyl-*trans*-decahydronaphthalen-r-1-ol (34c), the products of hydroboration of 8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalene (23a). Jones oxidation of the alcohols (33b) and (34c) gave 4a-methyl-*cis*- and *trans*-decahydronaphthalen-1-one (31a) and (32a), which on refluxing with isoprenyl acetate and a catalytic amount

4a-methyl-2,3,4,4a,5,6,7,8-octahydronaphth-1-yl acetate (23e). 4a-Methyl-*trans*-decahydronaphthalen-1-one (32a) was not readily seperable from its *cis*-isomer. A pure sample of 4a-methyl-*trans*-decahydronaphthalen-1-one (32a) was obtained by separation of c-4a-methyl-*cis*-decahydronaphthalen-r-1-ol (33b) and t-4a-methyl-*trans*-decahydronaphthalen-r-1-ol (34c) as the 1-acetates by preparative g.l.c. Reduction of the acetate (34a) to t-4a-methyl-*trans*-decahydronaphthalen-r-1-ol (34c) followed by oxidation with chromium trioxide-pyridine[37] gave the required ketone (32a).

The carbonium ion formed by rupture of the C(8a)-OH bond of t-8a-hydroxy-4a-methyl-*trans*-decahydronaphth-r-1-yl acetate (28h) in conformation (53, fig. 23) is destabilized by steric interaction between the axial C(1)-acetate and the methyl. It is significant that no c-4a-methyl-1,2,3,4,4a,5,6,7-octahydronaphth-r-yl acetate (23f) was observed in the reaction product.

The destabilizing influence of the C(1) acetate on the C(8a)-carbonium ion is sufficient to allow methyl migration to compete with regiospecific loss of one proton *syn* to the leaving group from conformer (54).

In contrast to this reaction, dehydration of t-8a-hydroxy-4a-methyl-*trans*-decahydronaphth-r-1-yl acetate (28h) in thionyl chloride-pyridine gave c-4a-methyl-1,2,3,4,4a,5,6,7-octahydronaphth-r-1-yl acetate (23f) as the only product. The p.m.r. spectrum of the product showed the C(8) vinyl proton as a triplet (J = 4Hz) centred at δ5.75 p.p.m. and the C(1)H as a multiplet centred at

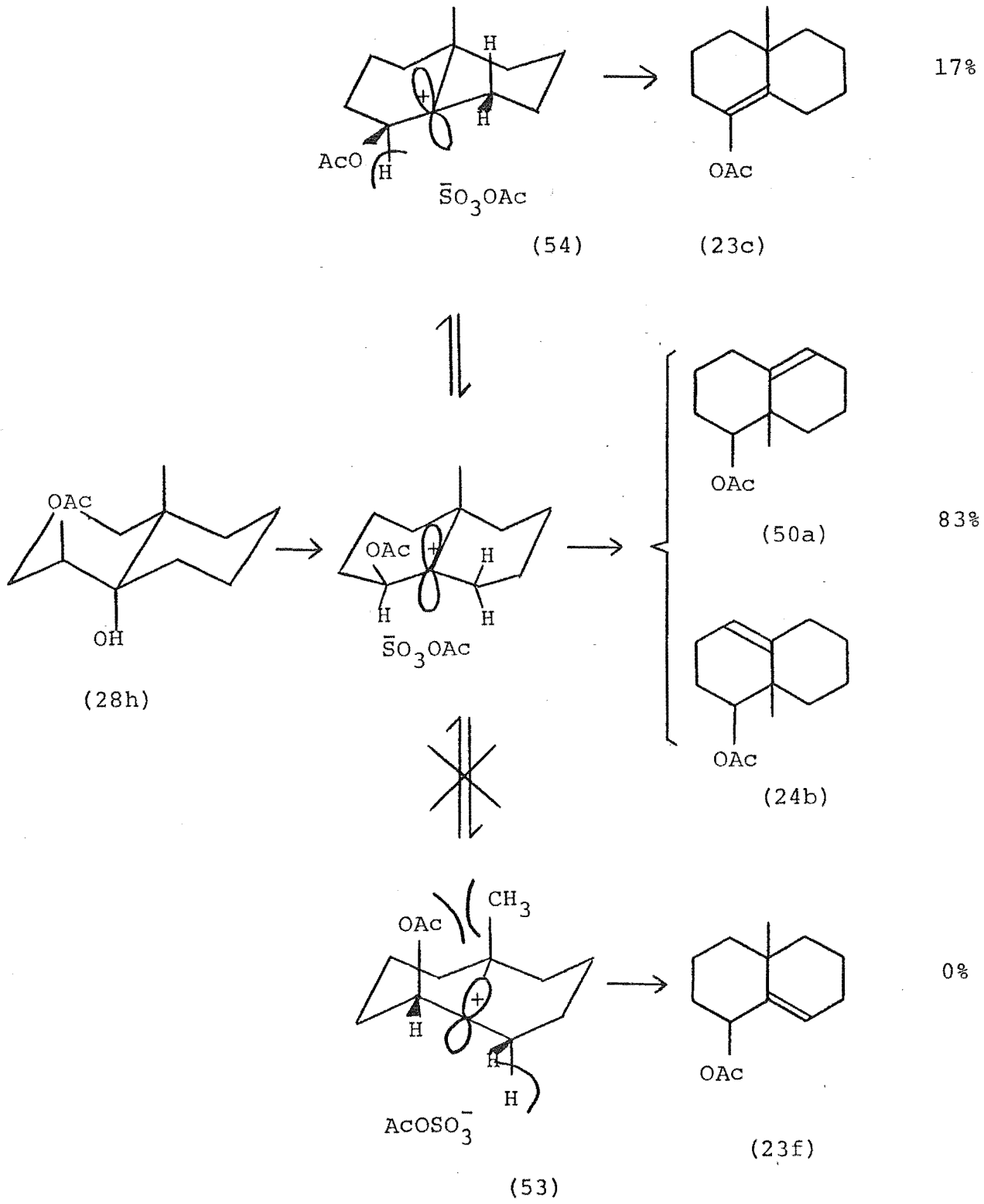

17%
AcO
H
H
H
$\bar{S}O_3OAc$
(54)
OAc
(23c)
OAc
(28h)
OAc
H
H
H
$\bar{S}O_3OAc$
OAc
(50a)
83%
OAc
(24b)
CH_3
OAc
H
H
H
$AcOSO_3^-$
(53)
OAc
(23f)
0%

Figure 23.

δ5.28 p.p.m. The methyl resonance at δ1.17 p.p.m., 0.37 p.p.m. downfield from the methyl resonance of *trans*-4a-methyldecahydronaphthalene (34b) is consistent with the assigned structure.[35] In the cholestane series the C(19)-methyl in 4β-acetoxycholest-5-ene (7b) absorbs 0.35 p.p.m. downfield from cholestane, whereas in 4α-acetoxycholest-5-ene (7a) the methyl is shifted downfield by 0.26 p.p.m.[36] The change in chemical shift of the methyl in the reaction product *c.f.* *trans*-4a-methyl-decahydronaphthalene (34b) shows that the configuration at C(1) has been retained during dehydration.

The dehydration of 8a-methyl-*trans*-decahydronaphthalen-r-4a-ol-t-5-*d* (28b) in thionyl chloride-pyridine has already been shown to occur regiospecifically, with loss of the C(4)H and C(5)H *anti*- to the leaving group (p.47). Similarly, no products arising from loss of the C(1)H *syn*- to the leaving group are observed in the product of reaction of t-8a-hydroxy-4a-methyl-*trans*-decahydronaphth-r-1-yl acetate (28h) with thionyl chloride-pyridine. Therefore it is thought that the c-4a-methyl-1,2,3,4,4a,5,6,7-octahydronaphth-r-1-yl acetate (23f) formed in this reaction arises from loss of the C(8)H *anti*- to the leaving group (fig. 24).

Reaction of steroidal C(5)- acetates with BF_3-acetic anhydride are believed to involve the intermediacy of carbonium ions. Reaction of 4a-methyl-*trans*-decahydro-r-1,t-8a-naphthylene diacetate (29b) with BF_3- acetic anhydride gave a 1:1 mixture of c-8a-methyl-1,2,3,4,6,7,8,8a-

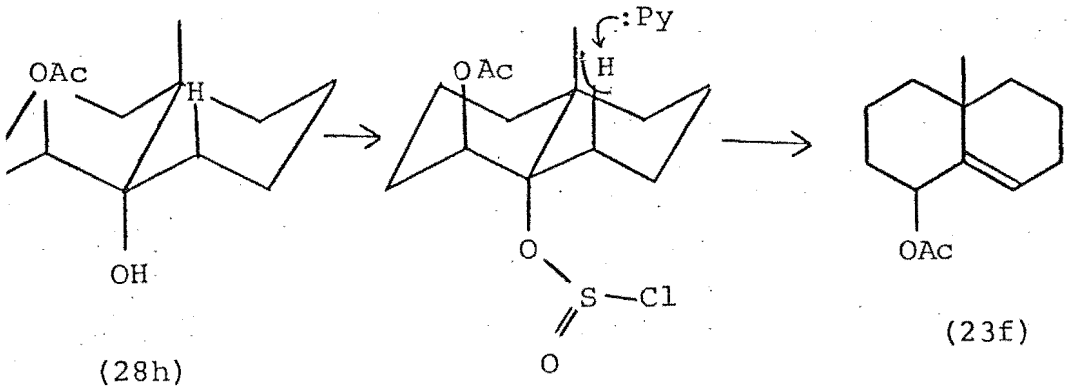


Figure 24.

octahydronaphth-r-1-yl acetate (24b) and c-8a-methyl-1,2,3,5,6,7,8a-octahydronaphth-r-1-yl acetate (50a). Also present in the product mixture was a small amount of ethylidene diacetate (55) identified by the identity of its p.m.r. spectrum with that of an authentic sample. In a seperate experiment, but in the absence of 4a-methyl-*trans*-decahydro-r-1,t-8a-naphthylene diacetate (29b) the reaction mixture afforded similar amounts (> 0.1%) of ethylidene diacetate (55).

The increase in yield of rearranged products in this reaction compared to the H_2SO_4-Ac_2O-HOAc catalysed dehydration of t-8a-hydroxy-4a-methyl-*trans*-decahydronaphth-r-1-yl acetate (28h) is consistent with similar observations in the steroid series but the precise reasons for the differences are a matter of speculation.

Rearrangement of 4a,5-epoxy-8a-methyldecahydronaphthalenes

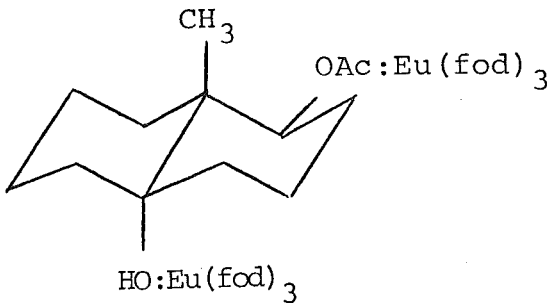
Boron trifluoride catalysed opening of an epoxide ring generates an electron deficient centre. Studies of acid catalysed reactions of steroidal 4,5- and 5,6-epoxides have been extensive and the results interpreted in terms of carbonium ion intermediates. Evidence for the intermediacy of carbonium ions follows from the observation that reaction products are produced in which the configuration at the reacting carbon is retained. For example reaction of 4β,5- and 5,6β-epoxy-5β-cholestane (56) and (57) with BF_3 etherate gave substantial amounts of appropriately substituted 5β-methyl-$\Delta^{13,17}$-cholestanes.[76] Migration of the C(10) methyl across the β- face of the molecule cannot occur in concert with C(5)-O bond breaking. Similarly, in a study of the aldehyde products obtained in rearrangements of a series of steroidal exocyclic-methylene epoxides it was found necessary to invoke the intermediacy of discrete ions.[77]

As part of the investigation of epoxy-decahydronaphthalenes an attempt was made to study the BF_3 catalysed rearrangements of 1,8a-epoxy-4a-methyl-*trans*-decahydronaphthalene (26a) and 1,8a-epoxy-4a-methyl-*cis*-decahydronaphthalene (25d). It was not possible to separate these isomers and a re-examination of reactions on the mixture afforded little new information.[35] The epimeric 4a,5-epoxy-c-8a-methyl-*cis*- and *trans*-decahydronaphth-r-1-yl acetates (25b) and (26c) were seperable and the BF_3 rearrangements

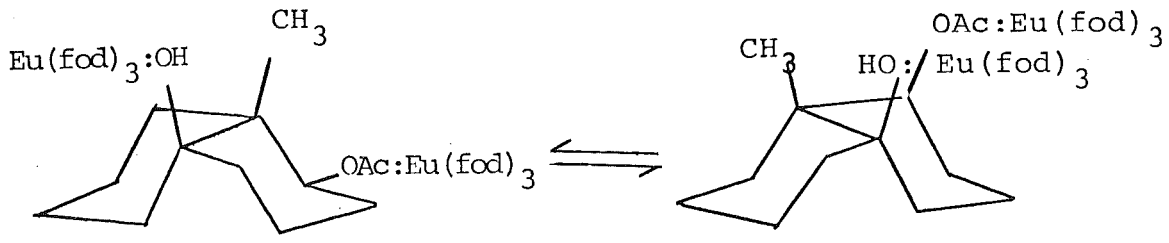
of these epoxides are included in this study.

A mixture (3:2) of 4a,5-epoxy-c-8a-methyl-*trans*-decahydronaphth-r-1-yl acetate (26c) and 4a,5-epoxy-c-8a-methyl-*cis*-decahydronaphth-r-1-yl acetate (25b) was obtained by epoxidation of c-8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphth-r-1-yl acetate (24b). The epimeric epoxy-acetates (26c) and (25b) were separated by chromatography on alumina and the sterochemistry was assigned on the basis of their p.m.r. spectra. The major component of the epoxide mixture exhibited a methyl signal at δ1.15 p.p.m. and the minor component a methyl signal at δ1.08 p.p.m. In the analogous steroid series the C(10) methyl resonance of 4β,5-epoxy-5β-cholestane (56) is 0.05 p.p.m. upfield of the C(10) methyl resonance of 4α,5-epoxy-5α-cholestane[61] (58). Similarly the C(10) methyl resonance of 5,6β-epoxy-5β-cholestane (57) is 0.25 p.p.m. upfield of the C(10) methyl resonance of 5,6α-epoxy-5α- cholestane[62] (59). The major epoxide was therefore assigned as 4a,5-epoxy-c-8a-methyl-*trans*-decahydronaphth-r-1-yl acetate (26c) and the minor component as 4a,5-epoxy-c-8a-methyl-*cis*-decahydronaphth-r-1-yl acetate (25b). This is also consistent with the major product resulting from attack by peracid on the least hindered face of the molecule. The stereochemistry was confirmed by L.A.H. reduction of each epoxide to give the corresponding diol which was characterised by p.m.r. shift studies. Reduction of the *trans*-epoxide (26c) with L.A.H. gave diol (60a)

which on acetylation afforded 4a-hydroxy-c-8a-methyl-*trans*-decahydronaphth-r-1-yl acetate (60b). Similar reduction of epoxide (25b) followed by acetylation gave 4a-hydroxy-c-8a-methyl-*cis*-decahydronaphth-r-1-yl acetate (61a). Successive amounts of $Eu(fod)_3$ shift reagent were added to these compounds and the spectra recorded. Both molecules possess two sites capable of coordinating with shift reagent (fig. 25). In the *trans*-hydroxy acetate (60b) the alcohol group is on the opposite side of the molecule to the methyl, while in the *cis*-isomer (61a) the alcohol and methyl groups are on the same side.



(60b)



(61a)

Figure 25.

A shift reagent molecule coordinated to the hydroxyl oxygen will have a marked effect on the chemical environment of the methyl for the *cis*-isomer (61a) and a lesser effect for the *trans*-isomer (60b). The effect of coordination of shift reagent to the acetate oxygen for these compounds on the position of the methyl resonances would be expected to be comparable. The effect of shift reagent is shown in fig. 26 and Table X. The effect of the shift reagent in the *trans*-isomer is about half that observed for the *cis*-isomer. This confirms the assigned stereochemistry of the epoxides (26c) and (25b) from which these alcohols were derived, and hence the epoxides (26c) and (25b) can be unambiguously assigned.

Reaction of 4a,5-epoxy-c-8a-methyl-*cis*-decahydronaphth-r-1-yl acetate (25b) with BF_3-etherate in benzene gave 8a-methyl,1,2,3,7,8,8a-hexahydronaphth-r-1-yl acetate (62a, 30%); c-8a-methyl-5-oxo-*trans*-decahydronaphth-r-1-yl acetate (32b, 26%); and 4a-fluoro-c-5-hydroxy-c-8a-methyl-*trans*-decahydronaphth-r-1-yl acetate (60c, 40%). An aldehyde, possibly the ring contracted compound (63, 4%) was shown to be present in the crude reaction product by a singlet at δ9.70 p.p.m. in the p.m.r. spectrum. Samples of this material could not however be separated from the reaction mixture.

The diene (62a) and ketone (32b) were separated by preperative g.l.c. The fluorohydrin (60c) could not be recovered by preparative g.l.c. and was isolated by dry column chromatography. The identity of the diene,

Figure 26: The chemical shift changes in compounds (61a) = □ and (60b) = O on adding $Eu(fod)_3$

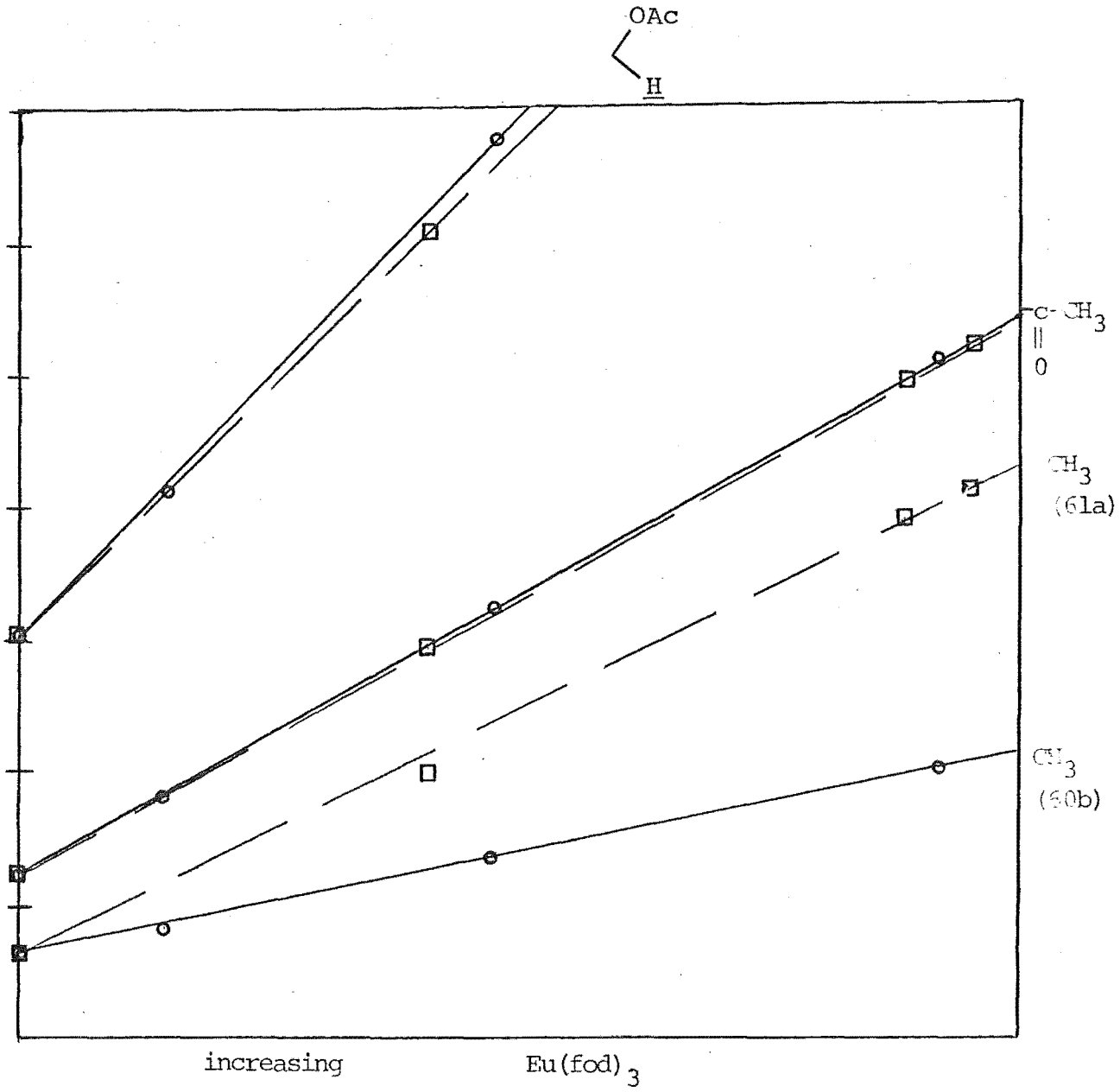


TABLE X

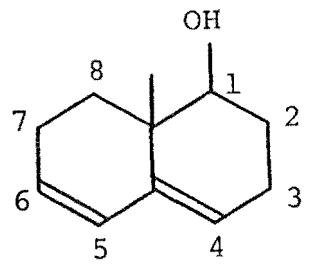
Shift Rate[a]

proton	cis-isomer (61a)	trans-isomer (60b)
C(1)H	1.7	1.8
CH_3-C- (O)	1.0	1.0
CH_3	0.86	0.35

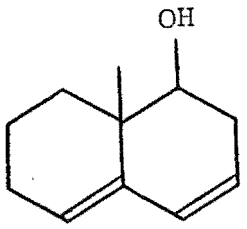
a Shift rate = $\frac{\text{change in chemical shift}}{\text{amt. } Eu(fod)_3}$, relative to CH_3-C- .

$\frac{M}{e}$ 206, was established on the basis of the U.V. and p.m.r. spectra. The U.V. spectrum consisted of a multiplet with maxima at 227 nm, ε22300; 234 nm, ε22600; 243 nm, ε14900, consistent with the presence of a conjugated diene chromophore.

In the p.m.r. spectrum the methyl resonance at δ1.07 p.p.m. compares with a value of δ0.96 for the C(10) methyl of cholesta-3,5-diene.[74] The 1-acetoxy substituent causes a similar downfield shift (ca. 0.1 p.p.m.) in other compounds in this series. Integration of the broad olefinic signal centred at δ5.68 shows the presence of three vinyl protons. Reduction of the acetoxy-diene (62a) with L.A.H. gave c-8a-methyl-1,2,3,7,8,8a-hexahydronaphthalen-r-1-ol (62b). Decoupling experiments on the p.m.r. spectrum after the addition of $Eu(fod)_3$ were used to distinguish between the two possible structures (62b) and (64) for this compound. The C(1)H



(62b)



(64)

Figure 27.

and $C(2)H_2$ are readily identifiable in the p.m.r. spectrum and exhibit large changes in chemical shift on addition of $Eu(fod)_3$ (figs. 27 and 28). After addition of $Eu(fod)_3$, C(1)H appeared at 20.8 p.p.m.; $C(2)H_2$ at 12.7 p.p.m.; the vinyl protons at 8.2-8.05 p.p.m.; and the remaining methylenes at 5.65 p.p.m., 4.83 p.p.m. and 4.0 p.p.m. For structure (62b) and $C(2)H_2$ would be coupled with the C(1)H and a methylene; for structure (64) $C(2)H_2$ would be coupled with C(1)H and a vinyl proton. Irradiation of the methylene at 5.65 p.p.m. caused the $C(2)H_2$ multiplet to collapse to a doublet, identifying the methylene as belonging to C(3) and the diene as having structure (62b). Confirmatory evidence was supplied by the observation that irradiation of the vinyl resonances had no effect on the C(2) methylene pattern, while irradiation of the C(2) protons reduced by one half the width at half height of the C(3) methylene peak. The coupling between the C(1) and C(2) protons was demonstrated by double irradiation experiments.

The ketone (32b) has absorptions at 1740 cm^{-1} (OAc) and 1715 cm^{-1} in the carbonyl region of the I.R. spectrum. In the p.m.r. spectrum the methyl signal at δ0.85 p.p.m. compares with the methyl signal of 4a-methyl-*trans*-decahydronaphthalen-1-one (32a) (δ0.80 p.p.m.). Incorporation of a C(1)-acetoxy substituent causes a downfield shift of the methyl signal of up to 0.07 p.p.m. for other compounds in this series and between 0.05 and 0.15 p.p.m. in steroids.[61,62] Equilibration of the ketone on dry column alumina produced a 3:2 mixture of (32b)

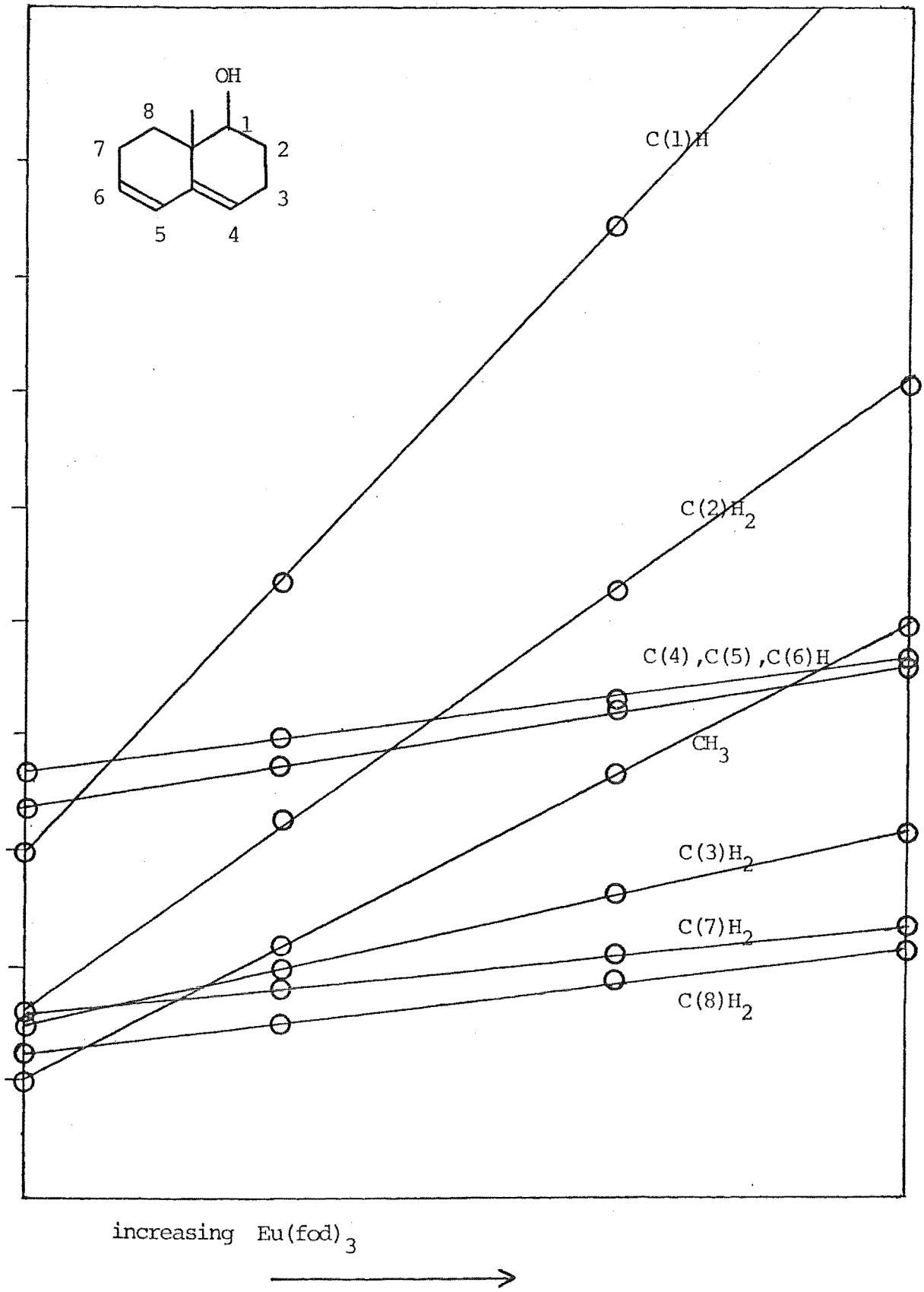

OH
8
1
7
2
6
3
5
4
C(1)H
C(2)H2
C(4),C(5),C(6)H
CH3
C(3)H2
C(7)H2
C(8)H2
increasing Eu(fod)3

Figure 28

and (31b), the minor component being the *cis* epimer (δ1.01(CH_3)).

The mass spectrum of the fluorohydrin (60c) exhibited a parent ion of mass 244, with a major peak at 224 (-HF). An I.R. absorption at 3525 cm^{-1} indicated the hydroxyl function. The methyl signal in the p.m.r. spectrum appeared as a doublet J_{F-H}1.5 Hz centred at δ1.24 p.p.m. While splitting of the methyl resonance due to a C(5) fluorine has not been reported for analogous steroid fluorohydrins, long range couplings to fluorine of this order have been observed for other systems.[78]

Rearrangement of 4a,5-epoxy-c-8-methyl-*cis*-decahydronaphth-r-1-yl acetate (25b) in ether with BF_3 etherate gave a mixture of c-8a-methyl-1,2,3,7,8,8a-hexahydronaphth-r-1-yl acetate (62a, 30%) and 4a-fluoro-c-5-hydroxy-c-8a-methyl-*trans*-decahydronaphth-r-1-yl acetate (60c, 70%) seperable by chromatography on alumina and identical (t.l.c., g.l.c., n.m.r.) with authentic samples.

Reaction of the epoxide (25b) in dioxane gave a mixture of the diene (62a, 46%); fluorohydrin (60c, 18%); ketone (32b, 8%); and six minor products (4%). The major components of the product mixture were identified by co-injection with authentic samples into several analytical g.l.c. columns.

Rearrangement of 4a,5-epoxy-c-8a-methyl-*trans*-decahydronaphth-r-1-yl acetate (26c) with freshly distilled BF_3 etherate in benzene gave a mixture of c-8a-methyl-1,2,3,7,8,8a-hexahydronaphth-r-1-yl acetate (62a, 34%); the ring contracted aldehyde (65, 6%);

c-8a-methyl-5-oxo-*cis*-decahydronaphth-r-yl acetate (31b, 7%), c-8a-methyl-5-oxo-*trans*-decahydronaphth-r-1-yl acetate (32b, 4%); an unidentified ketone (16%); 4a-fluoro-t-5-hydroxy-c-8a-methyl-*cis*-decahydronaphth-r-1-yl acetate (61b, 22%); and an unidentified polar compound (11%). The products were separated by preparative g.l.c.

The diene (62a) was shown by t.l.c., analytical g.l.c., and spectral data to be identical with the diene isolated from the *cis*-epoxide (25b) rearrangement. The aldehyde was tentatively assigned structure (65) on the basis that its p.m.r. spectrum has a singlet at δ9.4 (CHO) and a methyl signal at δ1.07, comparable to the analogous steroid aldehyde[73] (66). The *cis*- and *trans*- ketones (31b) and (32b) were found to equilibrate on active alumina. The *trans*- ketone (32b) was found to be identical by g.l.c. and spectral data to the ketone obtained from the rearrangement of the *cis*- epoxide (25b). The identity of the fluorohydrin follows from the presence of ions at 244 ($C_{13}H_{21}O_3F$), and 224 (parent-HF), and 184 (parent -HOAc) in the mass spectrum. The methyl peak in the p.m.r. spectrum occurs as a doublet (J CH_3, F 4 HZ) at δ1.01 p.p.m.

It is possible that the unidentified ketone could be one of the ring expanded compounds (67, 68), a consequence of migrationof the C(4a)- C(8a) and C(4)-C(4a)- bonds respectively to a C(5) carbonium ion (fig. 29). The formation of an A-nor-B-homo steroid

from a 4,5-epoxycholestane derivative is known to occur[80] however the p.m.r. shifts of the C(10) methyl in A-nor-B-homo cholestanes (68a) and (68b) (δ0.67 and δ1.07 respectively) are dissimilar to that observed for the unidentified ketone[80,81] (δ0.87).

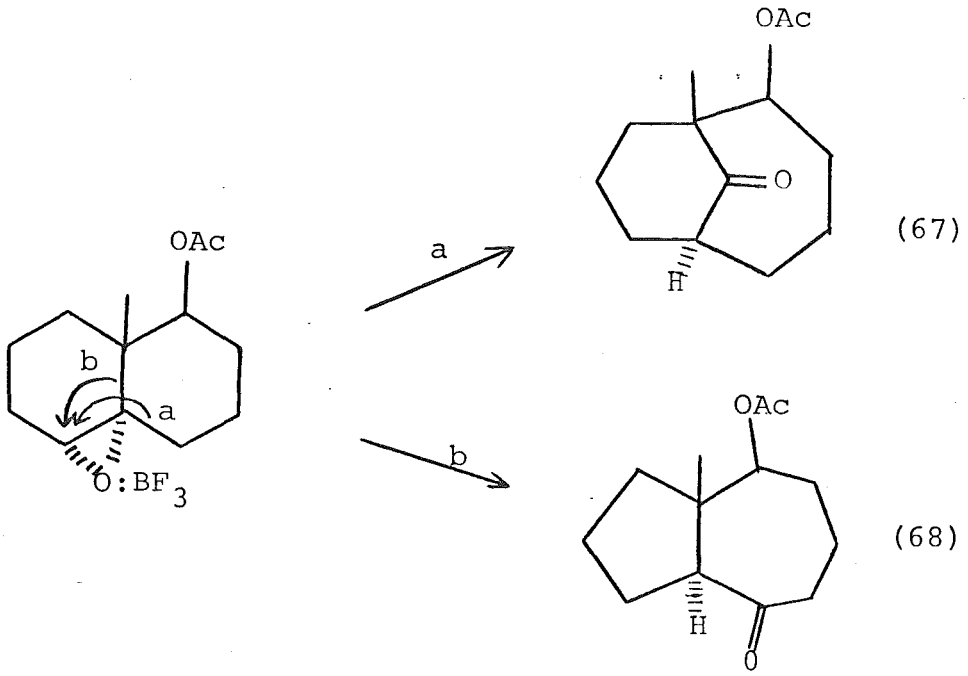


Figure 29.

In an attempt to obtain more information on the unidentified compounds, the rearrangement products were treated with methanolic KOH. This however resulted in a complex mixture of products. Under these conditions c-8a-methyl-5-oxo-*cis*-decahydronaphth-r-1-yl acetate (31b) and c-8a-methyl-5-oxo-*trans*-decahydronaphth-r-1-yl acetate (32b) both gave mixtures of r-1-hydroxy-c-8a-methyl-*cis*- and *trans*- decahydronaphthalen-5-one (31c) and (32c).

In contrast to the rearrangements of 4β,5- and 5,6β- epoxy-5β-cholestanes (56) and (57), no products of methyl migration were observed in the rearrangement of 4a,5-epoxy-c-8a-methyl-*cis*-decahydronaphth-r-1-yl acetate (25b). This is presumed to be due to the destabilizing electronic effect the C(1)- acetoxy group would have on the developing C(8a) carbonium ion, thus inhibiting migration of the C(8a) methyl. The diene probably occurs *via* dehydration of c-5-hydroxy-8a-methyl-1,2,3,5,6,7,8,8a-octahydronaphth-r-1-yl acetate (69) or its BF_3 coordinated counterpart, under the reaction conditions.

The increased yield of fluorohydrin in the slower reaction in ether is in line with trends observed for analogous steroid compounds.[82] The high yield of diene in the dioxane reaction may be due to an increase in the ability of the solvent to act as a base for abstraction of a C(4) proton to give the allylic alcohol (69), which subsequently undergoes dehydration to give the diene.

Conclusion

Dehydration of 8a-methyl-*cis*-decahydronaphthalen-4a-ol and 8a-methyl-*trans*-decahydronaphthalen-4a-ol in H_2SO_4-Ac_2O-AcOH has been found to occur regiospecifically without skeletal rearrangement or methyl migration, by abstraction of a proton *syn* to the leaving group. These results are best rationalized in terms of the intermediacy

of a tight ion pair where the departing oxy-anion acts as the base in the removal of a *syn* proton. The k_H/k_D of 2.2 ± 0.4 determined for the dehydration of 8a-methyl-*trans*-decahydronaphthalen-r-4a-ol-c-5-*d* in H_2SO_4-Ac_2O-AcOH demonstrates that conformational equilibration of the carbonium ion conformers is competitive with proton loss. The generality of this mechanism has been shown by the observation of similar regiospecificity in the H_2SO_4-Ac_2O-AcOH promoted dehydration of 5α-cholestan-5-ol-4α-*d*. In the reaction of t-8a-hydroxy-4a-methyl-*trans*-decahydronaphth-r-1-yl acetate with H_2SO_4-Ac_2O-AcOH the destabilizing effect of the C(1)-acetate on the C(8a)-ion is sufficient to allow migration of the C(4a)-methyl to compete with proton loss. Reaction of 4a-methyl-*trans*-1,8a-naphthalene diacetate with BF_3-acetic anhydride gives a higher yield of products of C(4a)-methyl migration than H_2SO_4-Ac_2O-AcOH dehydration of the corresponding C(8a)-alcohol, a trend previously observed in steroid studies. However, the presence of an acetoxy substituent adjacent to the methyl suppresses methyl migration, as shown by the absence of products of C(8a)-methyl migration in the rearrangement of 4a,5-epoxy-c-8a-methyl-*cis*-decahydronaphth-r-1-yl acetate (25b) with BF_3-etherate.

In contrast to the dehydration of 8a-methyl-*cis*- and *trans*-decahydronaphthalenes (27b) and (28b) in H_2SO_4-Ac_2O-Ac, a proton *anti* to the leaving group

is lost when alcohols (27b) and (28b) are treated with $SOCl_2$-pyridine. This is consistent with elimination occurring by an E2 mechanism. The kinetic isotope effect (k_H/k_D of 1.3 and 1.88 respectively) for these reactions indicates that the transition states in the reactions are unsymmetric, there being little C-H cleavage in the transition state.

EXPERIMENTAL

Infrared spectra were recorded on a Shimadzu IR27G spectrophotometer, ultraviolet spectra on a Varian Techtron 635 U.V. Spectrometer for cyclohexane solutions, and p.m.r. spectra on a Varian A60 and T60 spectrometer for $CDCl_3$ solutions with $CHCl_3$ and TMS as internal standards. C.m.r. spectra were recorded on a Varian CFT20 spectrometer equipped with a Sykes compucorder for $CDCl_3$ solutions with $CHCl_3$ and TMS as internal standards. Mass spectra were recorded on an A.E.I. MS902 spectrometer. Alumina used for chromatography was Spence grade H, deactivated by the addition of 10% v/v of 10% acetic acid and for dry column chromatography I.C.N. Pharmaceuticals Brockmann activity III/20 was used. Analytical g.l.c. was performed on a Varian Aerograph models 1200 and 2100. An Aerograph autoprep 705 and PYE series 105 were used for preparative scale gas liquid chromatography.

4a-Methyl-2,3,4,4a,5,6,7,8-octahydronaphthalen-2-one (19)

A mixture of 2-methylcylohexanone (21, 49 ml), methyl vinyl ketone (20, 42 ml) and conc.sulphuric acid (0.3 ml) was heated under reflux for 16 hours.[29] The reaction product was taken up in petroleum ether, washed with KOH (250 ml) and dried. The solvent and excess 2-methylcyclohexanone were removed under vacuum and the residue adsorbed onto alumina (500g). Elution

with ether (5%) in pentane afforded 4a-methyl-2,3,4,4a,5,6,7,8-octahydronaphthalen-2-one (19, 40g). b.p. 105-107° (4 torr.), ν_{max} 1682 cm^{-1}, P.m.r. δ1.22 (CH_3), 5.52 ($W\frac{h}{2}$ 4 Hz; C(1)H) (M^+ 164 $C_{11}H_{16}O$ requires 164).

4a-Methyl-2,3,4,4a,5,6,7,8-octahydronaphth-1-yl acetate (70)

To a stirred solution of LAH (5g) in dry ether (1ℓ) was slowly added a solution of 4a-methyl-2,3,4,4a,5,6,7,8-octahydronaphthalen-2-one (19,35g) in dry ether (100 ml). The reaction was stirred for two hours then quenched by the careful addition of $Na_2SO_4.10H_2O$ followed by water (0.5 ml). The solution was filtered and the solvent removed under reduced pressure. The residue (35g) was dissolved in pyridine (250 ml) and acetic anhydride (30 ml) added. The solution was kept at room temperature for 20 hours, then taken up in ether (1.5 l), washed with 2% aqueous H_2SO_4 (12 x 250 ml), dried, and the solvent removed under reduced pressure to give 4a-methyl-2,3,4,4a,5,6,7,8-octahydronaphth-1-yl acetate (70, 40g) as gum, ν_{max} 1730, 1245, 1025 cm^{-1} (lit.[27] 1736, 1247, 1021 cm^{-1}).

8a-Methyl-1,2,3,4,6,7,8,8a-octahydronaphthalene (23a)

A solution of 4a-methyl-2,3,4,4a,5,6,7,8-octahydronaphth-1-yl acetate (70, 40g) in dry ether (50 ml) was added to a stirred mixture of anhydrous ethylamine (250 ml) and freshly extruded lithium (4 gm) in a vessel equipped with an ammonia condenser, at a rate such that a deep blue

colour persisted throughout the addition [27, 83,84]. The mixture was stirred for a further 30 mins then transferred to a separating funnel (5 l) containing pentane (2 l) and washed with water (5 x 500 ml). The combined washings were extracted with pentane, the pentane fractions combined and the solvent removed under reduced pressure. The residue was distilled (ca. 100° at 26 torr) and the distillate redistilled on a Nester Faust teflon spinning band distillation column (pot temperature 120°, column temperature 88°, at 26 torr) to give 8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalene (23a, 10g), ν_{max} 1665, 1003, 985 cm^{-1} (lit[27] 1664, 1005, 985 cm^{-1}), P.m.r. δ1.05 (CH_3), 5.25 ($W_{\frac{h}{2}}$ 7 Hz; C(5)H), (C, 87.92, H, 12.08. $C_{11}H_{18}$ requires C, 87.93, H, 12.07).

1,8a-Epoxy-4a-methyldecahydronaphthalenes (25a) and (26a)

To an ether solution of monoperoxyphthalic acid prepared by treatment of phthalic anhydride (10g) in ether (170 ml) with hydrogen peroxide (100 vol, 17 ml) was added 8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalene (23a), (5 gm). After stirring for 5 mins at room temperature the reaction was quenched by washing with aqueous sodium bicarbonate (3 x 200 ml). The solvent was removed under reduced pressure and the residue adsorbed onto alumina (150 g). Elution with pentane afforded the *cis*- and *trans*- 1,8a-epoxy-4a-methyldecahydronaphthalenes (25a) and (26a) (4.2g), ν_{max} 925, 895, 838 cm^{-1} (lit[27] 925, 896, 838 cm^{-1}) P.m.r. δ1.06 (CH_3 *cis*-epoxide), 1.12

(CH_3 *trans*-epoxide), 2.78 ($W\frac{h}{2}$ 5 Hz; C(1)H) (lit[27] δ1.06, 1.12, 2.86-2.72).

8a-Methyl-*cis* and *trans*-decahydronaphthalen-4a-ols (27a) and (28a)

A solution of 1,8a-epoxy-4a-methyl-*cis*- and *trans*-decahydronaphthalene (750 mg) in dry ether (5 ml) was added to a mixture of L.A.H. (*ca.* 500 mg) in dry ether (50 ml) and the mixture stirred for three hours at room temperature. After careful addition of $Na_2SO_4.10H_2O$ and water the solution was filtered and the solvent removed. The residue was adsorbed onto a dry column of alumina (75g) and the column developed with $CHCl_3$. Segments of the column were removed and after extraction with ether afforded 8a-methyl-*cis*-decahydronaphthalen-4a-ol (27a) (150 mg). ν_{max} 3500, 1045, 998 cm^{-1} (lit[27] ν_{max} 1047, 1000 cm^{-1}), P.m.r. δ0.96 (CH_3) (lit[27] δ0.96). (M^+ 168.1507. $C_{11}H_{20}O$ requires 168.1514) and 8a-methyl-*trans*-decahydronaphthalen-4a-ol (28a) (250 mg), ν_{max} 3500, 1170, 1050, 883 cm^{-1}, P.m.r. δ1.03 (CH_3) (lit[27] δ1.02). (M^+ 168.1509. $C_{11}H_{20}O$ requires 168.1514).

8a-Methyl-*cis*- and *trans*-decahydronaphthalen-r-4a-ol-t-5-*d* (27b) and (28b)

To a mixture (*ca.* 2:3) of 1,8a-epoxy-4a-methyl-*cis*- and *trans*- decahydronaphthalene (25a) and (26a) (2g) in dry tetrahydrofuran was added LAD (0.5 g) and the mixture

heated under reflux for 24 hr. After careful addition of Na_2SO_4, $10H_2O$ and water the solution was decanted, dried, and after removal of solvent the residue was adsorbed onto alumina (200 g). Elution with pentane afforded 8a-methyl-*trans*-decahydronaphthalen-r-4a-ol-t-5-*d* (28b)(1.1g), ν_{max} 3500 cm^{-1}, P.m.r. δ1.02 (CH_3), 98.5 ± 2% mono-deuterated; m/e 190 (relative intensity 14.1) 169 (100), 168 (1.9) *cf.* 8a-methyl-*trans*-decahydronaphthalen-4a-ol m/e 169 (13.1), 168 (100), 167 (0.4). Further elution afforded mixed alcohol fractions (200 mg) followed by 8a-methyl-*cis*-decahydronaphthalen-r-4a-ol-t-5-*d* (27b)(700 mg), ν_{max} 3500 cm^{-1}, P.m.r. δ0.97 (CH_3), 99.6 ± 2% mono-deuterated; m/e 170(14.3), 169 (100), 168 (1.3) *cf.* 8a-methyl-*cis*-decahydronaphthalen-4a-ol m/e 169 (13.7), 168 (100), 167 (0.9).

4a-Methyl-*trans*-decahydronaphthalene-r-1,t-8a-diol (28c)

To a solution of *cis*- and *trans*- 1,8a-epoxy-4a-methyl decahydronaphthalene (2:3, 5 g) in tetrahydrofuran (250 ml) and water (100 ml) was added perchloric acid (2 ml) and the resulting mixture stirred for 2 hr. The product was extracted with dichloromethane and after removal of solvent adsorbed onto a dry column of alumina, and the column developed with ether. Segments of the column were removed and after extraction with dichloromethane afforded 4a-methyl-*trans*-decahydronaphthalene-r-1,t-8a-diol (28c) (2.24 g) crystallised from dichloromethane as

needles, m.p. 122.5 - 123.4°, ν_{max} 3500 cm^{-1}, P.m.r. δ1.23 (CH_3), 3.48 ($W_{\frac{h}{2}}$ 7 Hz, C(1)H) (Found: C, 71.7; H, 10.8. $C_{11}H_{20}O_2$ requires C, 71.7; H, 10.9%) and a mixture of this diol along with 4a-methyl-*cis*-decahydronaphthalene-r-1,t-8a-diol (1.5g). This mixture was separated by dry column chromatography to afford 4a-methyl-*trans*-decahydronaphthalene-r-1,t-8a-diol (640 mg) and 4a-methyl-*cis*-decahydronaphthalene-r-1,t-8a-diol (27c) (420 mg) as a gum, ν_{max} 3450 cm^{-1}, P.m.r. δ0.95 (CH_3), 2.72 ($W_{\frac{h}{2}}$ 6 Hz; OH), 3.80 ($W_{\frac{h}{2}}$ 14 Hz; C(1)H) (M^+ 184.1464. $C_{11}H_{20}O_2$ requires 184.1463).

8a-Methyl-*trans*-decahydronaphthalen-r-4a-ol-c-5-*d* (28g)

To a mixture of chromium trioxide (1.34 g), pyridine (2.1 ml) and dry methylene chloride[37] which had been allowed to stir for 15 min. was added a solution of 4a-methyl-*trans*-decahydronaphthalene-r-1,t-8a-diol (28c) (380 mg) in dichloromethane (5 ml). After 20 min. the reaction was poured into ether (50 ml), washed successively with aqueous bicarbonate, dilute sulphuric acid and brine, the ether solution dried over Na_2SO_4 and the solvent removed to give 8a-hydroxy-4a-methyl-*trans*-decahydronaphthalen-1-one (28d) (280 mg), ν_{max} 3480 cm^{-1}, P.m.r. δ0.83 (CH_3) (M^+ 182. $C_{11}H_{18}O_2$ requires 182). contaminated with *ca* 5% starting diol.

A solution of 8a-hydroxy-4a-methyl-*trans*-decahydronaphthalen-1-one (28d) (300 mg) in dry tetrahydrofuran

(5 ml) was added to a solution of LAD (150 mg) in tetrahydrofuran (50 ml) and the mixture stirred for 26 hr at room temperature. After careful addition of Na_2SO_4, $10H_2O$ and water the solution was decanted, dried and after removal of solvent afforded 4a-methyl-*trans*-decahydronaphthalene-r-1,t-8a-diol-1-*d* (28e) (290 mg), ν_{max} 3500 cm^{-1}, P.m.r. δ1.23 (CH_3).

To a solution of 4a-methyl-*trans*-decahydronaphthalene-4-1,t-8a-diol-1-*d* (290 mg) in dry pyridine (12 ml) was added methanesulphonyl chloride and the mixture stirred for four days at room temperature. The reaction mixture was poured into ether and washed successively with aqueous bicarbonate, dilute sulphuric acid and brine. After removal of the solvent the residue was adsorbed onto alumina. After 2 hr elution with pentane afforded 1,8a-epoxy-4a-methyl-*trans*-decahydronaphthalene-1-*d* (26b) (190 mg), P.m.r. δ1-03 (CH_3) identical by glc and tlc with undeuterated authentic sample. Elution with ether gave starting diol (80 mg), ν_{max} 3500 cm^{-1}, P.m.r. δ1.23 (CH_3).

A solution of 1,8a-epoxy-4a-methyl-*trans*-decahydronaphthalene-1-*d* (26b) (180 mg) in dry ether (5 ml) was added to a solution of LAH (0.2 g) in dry ether (25 ml) and the mixture heated under reflux for 1 hr. The product was isolated in the usual manner and adsorbed onto alumina (25 g). Elution with ether-pentane (1:20) gave 8a-methyl-*trans*-decahydronaphthalen-4a-ol-c-5-*d* (28h) (180 mg), ν_{max} 3500 cm^{-1}. P.m.r. δ1.03

(CH_3) (M^+ 169.1576. $C_{11}H_{19}$ DO requires 169.1577) m/e 170 (relative intensity 26), 169 (100) 168 (7) *cf.* 8a-methyl-*trans*-decahydronaphthalen-4a-ol m/e 169 (13.1), 168 (100), 167 (0.4)). The mass spectrum indicates, unlabelled : mono- : di- deuterated alcohol in the ratio 5.5 : 83.5 : 11.0.

t-8a-Hydroxy-4a-methyl-*trans*-decahydronaphth-r-1-yl acetate (28h)

A solution of 4a-methyl-*trans*-decahydronaphthalene-r-1,t-8a-diol (28c) (1.95 g) in pyridine (15 ml) and acetic anhydride (2 ml) was kept at room temperature for 24 hours. The product was isolated by means of ether and recrystallised from ether to give t-8a-hydroxy-4a-methyl-*trans*-decahydronaphth-r-1-yl acetate (28h) (1.52 g) as needles, m.p. 87 - 88°, ν_{max} 3550, 1725 and 1238 cm^{-1}. P.m.r. δ1.18 (CH_3), 2.05 ($OCOCH_3$), 4.66 ($W_{\frac{h}{2}}$ 7 Hz; C(1)H) (M^+ 226.1569. $C_{13}H_{22}O_3$ requires 226.1568).

4a-Methyl-*trans*-decahydro-r-1,t-9-naphthylene diacetate (29b)

To a solution of t-8a-hydroxy-4a-methyl-*trans*-decahydronaphth-r-1-yl acetate (28h) (470 mg) in chloroform (15 ml) was added freshly distilled N,N-dimethylaniline (1.6 ml) and acetyl chloride (1.6 ml) and the mixture heated under reflux for 28 hr. The mixture was poured into ether (100 ml) and washed successively with aqueous bicarbonate, dilute sulphuric acid and water. After removal

of the solvent the residue was adsorbed onto alumina (30g). Elution with pentane gave 4a-methyl-*trans*-decahydro-r-1,t-8a-naphthylene diacetate (29b) (350 mg) crystallised as needles from pentane, m.p. 86 - 88°, ν_{max} 1755, 1236 and 1220 cm^{-1}, P.m.r. δ1.23 (CH_3), 2.03 and 2.07 ($OCOCH_3$'s), 5.78 ($W_{\frac{1}{2}}^{h}$ 4 Hz; C(1)H) (M^+ 268. $C_{15}H_{24}O_4$ requires 268, M^+-60 208.1459, $C_{15}H_{24}O_4$ - $C_2H_4O_2$ requires 208.1463).

AcOH-Ac_2O-H_2SO_4 dehydration of;

(a) 8a-methyl-*trans*-decahydronaphthalen-r-4a-ol-t-5-*d* (28b). To a stirred solution of 8a-methyl-*trans*-decahydronaphthalen-r-4a-ol-t-5-*d* (28b) (450 mg) in acetic acid (16 ml) - acetic anhydride (4 mls) was rapidly added a solution of sulphuric acid in acetic acid (4 ml; 1% V/V). After 20 sec. the solution was poured into pentane (200 ml) and saturated aqueous sodium bicarbonate (200 ml). Sodium bicarbonate was added with vigorous stirring until effervescence ceased. The pentane solution was further washed with aqueous bicarbonate, dried and after removal of solvent afforded a mixture (1:1) of 8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalene-5-*d* (23b) and r-8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalene-c-4-*d* (23c) (265 mg), ν_{max} 1665, 1603 and 985 cm^{-1}, P.m.r. δ1.05 (CH_3), 5.25 ($W_{\frac{1}{2}}^{h}$ 5Hz; vinyl H: ½H), m/e 152 (relative intensity 13.0), 151 (100), 150 (4.7). (*c.f.* 8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalene m/e 151 (12.4), 150 (100), 149 (2.1)) i.e. 97.5 ± 4% retention of label.

(b) 8a-methyl-*trans*-decahydronaphthalen-r-4a-ol-c-5-*d* (28g)

A solution of 8a-methyl-*trans*-decahydronaphthalen-r-4a-ol-c-5-*d* (28g) containing 5.5% undeuterated and 11% di-deuterated alcohol (180 mg) in acetic acid - acetic anhydride - sulphuric acid was reacted as above to give a reaction product mixture, ν_{max} 1665 cm^{-1}, P.m.r. δ1.05 (CH_3), 5.25 ($W_{\frac{1}{2}}^{h}$ 7 Hz; C(1)H, 1H), m/e 152 (relative intensity 24), 151 (100) and 150 (52). Allowing for undeuterated and dideuterated alcohols in the starting mixture the data indicates that alcohol (28g) affords 8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalene (23a) and r-8a-methyl-1,2,3,4,6,7,8,8a-ocathydronaphthalene-t-5-*d* (23d) in the ratio 1.0 : 2.2 (± 0.4).

(c) 8a-methyl-*cis*-decahydronaphthalen-r-4a-ol-t-5-*d* (27b)

A solution of 8a-methyl-*cis*-decahydronaphthalen-r-4a-ol-t-5-*d* (27b)(450 mg) in acetic acid - acetic anhydride - sulphuric acid was reacted as above to give a mixture (1:1) of r-8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalene -5-*d* and -t-4-*d* (23b) and (23d), ν_{max} 1665 cm^{-1} P.m.r. δ1.05 (CH_3), 5.25 ($W_{\frac{1}{2}}^{h}$ 6 Hz; C(1)H, ½H), m/e 152 relative intensity 13.2, 151 (100), 150 (6) i.e. 6.2 ± 4% retention of label.

(d) 5α-cholestan-5-ol-4α-*d* (3f)

A solution of 5α-cholestan-5-ol-4α-*d* (3f, 198 mg) in acetic acid - acetic anhydride - sulphuric acid was allowed to react for 20 sec as above to give a 1:1 mixture of Δ^4-cholestene (14a) and Δ^5-cholestene-4α-*d*

(7d)(102 mg), $[\alpha]_d$ + 6.4° P.m.r. δ0.68 (C(18)H_3) 0.99 (C(19)H_3), 5.27 ($W_{\frac{1}{2}}^h$ 8Hz, C(4)H and C(6)H), (M^+ 371, 370. $C_{27}H_{45}D$ requires 371, $C_{27}H_{46}$ requires 370).

(e) t-8a-hydroxy-4a-methyl-*trans*-decahydronaphth-r-1-yl acetate (28h)

A solution of t-8a-hydroxy-4a-methyl-*trans*-decahydronaphth-r-1-yl acetate (28h) (640 mg) in acetic acid - acetic anhydride - sulphuric acid was allowed to react for 30 sec. as above to give a product mixture (400 mg), ν_{max} 1740 and 1232 cm^{-1} shown to contain 4a-methyl-*trans*-decahydronaphthalen-1-one (32a) (*ca.* 8%), P.m.r. δ0.78 (CH_3), 4a-methyl-2,3,4,4a,5,6,7,8-octahydronaphth-1-yl acetate (23e) (*ca.* 8%), P.m.r. δ1.10 (CH_3) 2.08 (OAc), c-8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphth-r-1-yl acetate (24b) (*ca.* 50%), P.m.r. δ1.07 (CH_3), 2.02 (OAc), 4.55 ($W_{\frac{1}{2}}^h$ 20 Hz, C(1)H) 5.42 ($W_{\frac{1}{2}}^h$ 9 Hz, C(5)H) and c-8a-methyl-1,2,3,5,6,7,8,8a-octahydronaphth-r-1-yl acetate (50a) (*ca.* 33%), P.m.r. δ1.08 (CH_3), 2.02 (OAc), 4.55 ($W_{\frac{1}{2}}^h$ 20 Hz, C(1)H), 5.02 ($W_{\frac{1}{2}}^h$ 10 Hz, C(4)H). The product mixture could not be separated and was dissolved in dry ether 50 ml and allowed to react with LAH (0.5 g) for 1 hr. The product mixture isolated in the usual manner was partially separated by preparative g.l.c. (22 ft carbowax 20M at 140°) to give c-4a-methyl-*trans*-decahydronaphthalen-r-1-ol (34c) (52 mg), ν_{max} 3500 cm^{-1}. P.m.r. δ1.07 (CH_3), 3.78 ($W_{\frac{1}{2}}^h$ 8 Hz; C(1)H) (M^+ 168.1514 . $C_{11}H_{20}O$ requires 168.1514) (lit.cit.[36] δ1.07, 3.80 ($W_{\frac{1}{2}}^h$ 8 Hz)) and

a mixture (ν_{max} 3400 and 1655 cm^{-1}; M^+ 166 . $C_{11}H_{18}O$ requires 166) of c-8a-methyl-1,2,3,5,6,7,8,8a-octahydronaphthalen-r-1-ol (50b) P.m.r. δ1.00 (CH_3), 3.37 ($W\frac{h}{2}$ 20 Hz; C(1)H), 5.02 ($W\frac{h}{2}$ 8 Hz; C(4)H) and c-8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalen-r-1-ol (24a) P.m.r. 1.03 (CH_3), 3.30 ($W\frac{h}{2}$ 17 Hz; C(1)H), 5.42 ($W\frac{h}{2}$ δ Hz; C(5)H). The mixture of hydroxy-olefins in acetone was oxidised with Jones reagent to give a mixture (3:2) of 8a-methyl-1,2,3,4,6,7,8,8a- and -1,2,3,5,6,7,8,8a-octahydronaphthalen-1-one (51) and (52) which were separable by repetitive preparative g.l.c. to give samples (*ca.* 90% pure) of: 4a,5-olefin (51), $\nu_{max}^{CS_2}$ 1710 cm^{-1}., λ_{max} 305 nm (ε64), 296 (68), 288 (63), 198 (4737), in cyclohexane, and 4,4a-olefin (52), $\nu_{max}^{CS_2}$ 1710 cm^{-1}., λ_{max} 304 nm (ε130), 298 (129), 198 (5120).

4a-Methyl-*cis*- and *trans*-1-decahydronaphthalen-1-ones (31a) and (32a)

Diborane in a stream of nitrogen was bubbled through a solution of 8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalene (23a) (1 g) in THF (20 ml) for 2 hr. The mixture was kept at room temperature for 12 hr then sodium hydroxide (50 ml: 10% w/v) and hydrogen peroxide (50 ml : 33%) was added and the mixture stirred for 1 hr. The product was isolated by means of ether to give a 3 : 7 mixture of t-4a-methyl-*trans*-decahydronaphthalen-r-1-ol (34c) and c-4a-methyl-*cis*-decahydronaphthalen-r-1-ol (33b) (920 mg), ν_{max} 3500 cm^{-1} P.m.r. δ1.0 (CH_3 *cis*);

0.82 (CH_3 *trans*). The mixture of alcohol in pyridine (10 ml) - acetic anhydride (1 ml) was kept at room temperature overnight. The product acetates were isolated by means of ether and preparative gas chromatography afforded t-4a-methyl-*trans*-decahydronaphth-r-1-yl acetate (34a) (89 mg), ν_{max} 1730 and 1242 cm^{-1}, P.m.r. δ0.88 (CH_3), 2.02 (OAc), 4.16 ($W_{\frac{1}{2}}^{h}$ 18 Hz; C(1)H) (M^+ 210. $C_{13}H_{22}O_2$ requires 210), and c-4a-methyl-*cis*-decahydronaphth-r-1-yl acetate (33a) (326 mg), ν_{max} 1725 and 1235 cm^{-1}, P.m.r. δ1.02(CH_3), 2.02 (OAc), 5.07 ($W_{\frac{1}{2}}^{h}$ 24 Hz; (C(1)H) (M^+ 210. $C_{13}H_{22}O_2$ requires 210).

To a solution t-4a-methyl-*trans*-decahydronaphth-r-1-yl acetate (34a) (89 mg) in ether (10 ml) was added LAH(50 mg) and the mixture stirred for 3 hr. Isolation of the product gave t-4a-methyl-*trans*-decahydronaphthalen-r-1-ol (34c)(65 mg) as an oil, ν_{max} 3500 cm^{-1}, P.m.r. δ0.82 (CH_3) 3.42 ($W_{\frac{1}{2}}^{h}$ 14 Hz; C(1)H) (M^+ 168.1512. $C_{11}H_{20}O$ requires 168.1514). A mixture of chromium trioxide (1 g) in dry pyridine (1.9 ml) and dry dichloromethane (25 ml) was stirred for 15 min. A solution of t-4a-methyl-*trans*-decahydronaphthalen-r-1-ol (34c) (60 mg) in dichloromethane (2 ml) was added and the resulting mixture stirred for 20 min. Isolation of the product gave 4a-methyl-*trans*-decahydronaphthalen-1-one (32a) (48 mg), ν_{max} 1715 cm^{-1}, P.m.r. 0.80 (CH_3)(M^+ 166.1359. $C_{11}H_{18}O$ requires 166.1357).

To a solution of c-4a-methyl-*cis*-decahydronaphth-r-1-yl acetate (33a) (300 mg) in dry ether (10 ml) was added L.A.H. (100 mg) and the resulting mixture stirred for 3 hr. Isolation of the product in the usual manner afforded c-4a-methyl-*cis*-decahydronaphthalen-r-4a-ol (33b)(235 mg), ν_{max} 3500 cm^{-1}, P.m.r. δ1.00 (CH_3), 3.78 ($W\frac{h}{2}$ 12 Hz; C(1)H) (M^+ 168.1511 $C_{11}H_{20}O$ requires 168.1514). To a mixture of chromium trioxide (1.3 g) in dry pyridine (2.1 ml) and dry dichloromethane (32 ml) which had been stirred for 15 min. was added a solution of c-4a-methyl-*cis*-decahydronaphthalen-r-4a-ol (33b) (220 mg) in dichloromethane (5 ml). The resulting mixture was stirred for 20 min. and the product isolated by means of ether to give 4a-methyl-*cis*-decahydronaphthalen-1-one (31a) (180 mg), ν_{max} 1710 cm^{-1}, P.m.r. δ0.98 (CH_3) (M^+ 166.1355 $C_{11}H_{18}O$ required 166.1357).

4a-Methyl-2,3,4,4a,5,6,7,8-octahydronaphth-1-yl acetate (23e)

A mixture of 4a-methyl-*cis*- and *trans*-decahydronaphthalen-1-ones (31a) and (32a) (300 mg) p-toluenesulphonic acid (50 mg) and isopropenyl acetate (10 ml) was kept at 100° for 17 hr and solvent (3 ml) slowly removed by distillation throught a Vigreux column (180 cm). The reaction mixture was poured into ether and washed with aqueous $NaHCO_3$. After removal of organic solvents, preparative g.l.c. afforded 4a-methyl-2,3,4,4a,5,6,7,8-octahydronaphth-1-yl acetate (23e) (47 mg), ν_{max} 1715 cm^{-1}.

2.08 (OAc) (M^+ 208 . $C_{13}H_{20}O_2$ requires 208); 4a-methyl-*cis*-3,4,4a,5,6,7,8,8a-octahydronaphth-1-yl acetate (37 mg), ν_{max} 1710 cm^{-1}. P.m.r. δ1.00 (CH_3), 2.10 (OAc), 5.25 (t, J 3 Hz; C(2)H), (M^+ 208 . $C_{13}H_{20}O_2$ requires 208), and 4a-methyl-*trans*-3,4,4a,5,6,7,8,8a-octahydronaphth-1-yl acetate (25 mg), ν_{max} 1715 cm^{-1}, P.m.r. δ0.88 (CH_3) 2.10 (OAc), 5.25 (d, J 3Hz; C(2)H) (M^+ 208.$C_{13}H_{20}O_2$ requires 208).

c-8a-Methyl-1,2,3,4,6,7,8,8a-octahydronaphthalen-r-1-ol (24a)

To a stirred solution of L.A.H. (8g) in dry ether (800 ml) was added a solution of 8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalene-1,6-dione[85](22) (50 g) in ether (200 ml) and the mixture heated under reflux for 4 hrs. The reaction was quenched by the addition of $NaSO_4.10H_2O$, the mixture filtered and the solvent removed. The residue was dissolved in pyridine (350 ml), acetic anhydride (50 ml) added and the solution kept for 24 hrs at room temperature. The solution was poured into ether (2 l) and washed with 2% H_2SO_4 (10 x 50 ml) and brine (2 x 200 ml). The solution was dried, the solvent removed, and the residue dissolved in dry tetrahydrofuran (50 ml). The solution was added dropwise to a flask containing anhydrous ethylamine (500 ml) and freshly extruded lithium metal[30] (*ca.* 5 g). The mixture was stirred for 4 hrs at 273 K. The reaction was quenched by the cautious addition of aqueous NH_4Cl and the solution extracted with ether (4 x 500 ml). The combined extracts were washed with aqueous Na_2CO_3

(2 x 200 ml), dried, and the ether removed. The residue was adsorbed onto alumina (700 g). Elution with benzene:pet. ether (1:10) gave c-8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalen-r-1-ol (24a, 5.5g), ν_{max} 3400, 1650, 1035 cm^{-1}, P.m.r. δ1.03 (CH_3), δ3.30 ($W_{\frac{1}{2}}^{h}$ 17 Hz; C(1)H) 5.42 ($W_{\frac{1}{2}}^{h}$ 8 Hz; C(5)H) (M^+ 166 . $C_{11}H_{18}O$ requires 166).

8a-Methyl-12,3,4,6,7,8,8a-octahydronaphthalen-1-one (51)

To a solution of c-8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalen-r-1-ol in acetone was added Jones reagent[86,87] (0.2 ml). After 20 min. the product was isolated and adsorbed onto alumina (10 g). Elution with ether-pentane (:50) gave 8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalen-1-one (51) as a gum, ν_{max} 1710, 1020 and 918 cm^{-1}, λ_{max} 304 nm (ε65), 296 (65), 199 (5000) (M^+ 164 . $C_{11}H_{16}O$ requires 164).

c-8a-Methyl-1,2,3,4,6,7,8,8a-octahydronaphth-r-1-yl acetate (24b)

A solution of c-8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalen-r-1-ol (2 g) in acetic anhydride (2 ml) and pyridine (10 ml) was kept at room temperature for 24 hrs. The product was isolated by means of ether and after the removal of solvent was adsorbed onto alumina (100 g). Elution with pentane gave c-8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphth-r-1-yl acetate (24b) as a gum (1.8 g), ν_{max} 1735 and 1225 cm^{-1}, P.m.r. δ1.07 (CH_3), 2.02 (OAc), 4.55 ($W_{\frac{1}{2}}^{h}$ 16 Hz; C(1)H), 5.42 ($W_{\frac{1}{2}}^{h}$ 9 Hz;

C(5)H) (M^+ 208 . $C_{13}H_{20}O_2$ requires 208).

Thionyl chloride-pyridine dehydration of;

(a) 8a-methyl-*trans*-decahydronaphthalen-r-4a-ol-t-5-*d* (28b). Thionyl chloride (3.5 ml) was added to a solution of 8a-methyl-*trans*-decahydronaphthalen-r-4a-ol-t-5-*d* (28b) (812 mg) in pyridine (50 ml) and the solution kept near freezing by periodic immersion in a dry ice - chloroform bath. After 10 min. the reaction mixture was poured into ether (150 ml) and washed successively with aqueous bicarbonate, dilute sulphuric acid and water. The ether solution was dried with anhydrous $MgSO_4$ and the solvent removed by distillation through a 6" vigreaux column to give a mixture (7:13) of 8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalene (23a and r-8a-methyl-1,2,3,4,6,7,8a-octahydronaphthalene-c-4-*d* (23c) (602 mg), ν_{max} 1665 cm^{-1}, P.m.r. δ1.05 (CH_3), 5.25 ($W_{\frac{1}{2}}^{h}$ 7 Hz, (C(1)H, 1H) (m/e 152 (relative intensity 12.1), 151 (100), 150 (51.7)).

(b) 8a-methyl-*cis*-decahydronaphthalen-r-4a-ol-t-5-*d* (27b). A solution of 8a-methyl-*cis*-decahydronaphthalen-r-4a-ol-t-5-*d* (27b) (450 mg) in pyridine (25 ml) was reacted as above with thionyl chloride (1.7 ml) to give a mixture (1:1.33) of 8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalene (23a) and r-8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalen-t-4-*d* (23d) (320 mg), ν_{max} 1665 cm^{-1}, P.m.r. δ1.05 (CH_3), 5.25 ($W_{\frac{1}{2}}^{h}$ 7 Hz, C(1)H, 1H) (m/e 152 (relative intensity 14.0), 151 (100), 150 (71.3).

(c) t-8a-hydroxy-4a-methyl-*trans*-decahydronaphth-r-1-yl acetate (28h). A solution of t-8a-hydroxy-4a-methyl-*trans*-decahydronaphth-r-1-yl acetate (28h) (67 mg) in pyridine was reacted as above with thionyl chloride to give c-4a-methyl-1,2,3,4,4a,5,6,7-octahydronaphth-r-1-yl acetate (23f) (39 mg), ν_{max} 1745 and 1232 cm^{-1}, P.m.r. δ1.17 (CH_3), 2.00 (OAc) 5.28 ($W\frac{h}{2}$ 5 Hz; C(1)H), 5.75 (t, J = 3 Hz, C(8)H) (M^+ 208 . $C_{13}H_{20}O_2$ requires 208).

Reaction of 4a-methyl-*trans*-decahydro-1,8a-naphthylene diacetate (29b) with BF_3-Ac_2O.

To a solution of 4a-methyl-*trans*-decahydro-1,8a-naphthylene diacetate (29b) (160 mg) in acetic anhydride (50 ml) was added freshly distilled BF_3-etherate (0.5 ml) and the mixture kept for 5 hr at room temperature. The solution was poured into a stirred mixture of ether (250 ml) and aqueous $NaHCO_3$. Bicarbonate was added until effervescence ceased. The ether layer was washed with water, dried and after removal of solvent gave a mixture (1:1) of c-8a-methyl-1,2,3,4,6,7,8,8a- and 1,2,3,5,6,7,8,8a-octahydronaphth-r-1-yl acetate (50a) and (24b) and starting diacetate (29b) contaminated with ethylidene diacetate (55). The mixture was absorbed onto alumina (10 g) and elution with pentane effected separation of the olefin mixture, ν_{max} 1740 and 1735 cm^{-1}, P.m.r. (4a,5-olefin) δ1.07 (CH_3), 2.02 (OAc), 4.55 ($W\frac{h}{2}$ 20 Hz; C(1)H), 5.42 ($W\frac{h}{2}$ 9 Hz; C(5)H), (4,4a-olefin) 1.12 (CH_3), 2.02 (OAc)

4.55 ($W_{\frac{1}{2}}^{h}$ 20 Hz; C(1)H), 5.27 ($W_{\frac{1}{2}}^{h}$ 8 Hz; C(4)H) and starting diacetate, m.p. 86 - 88°, ν_{max} 1755, 1236 and 1220 cm^{-1}.

Ethylidene diacetate (55)

A mixture of acetaldehyde (16g), acetic anhydride (9 g) and conc. sulphuric acid (2 drops) was kept at 273 K for 12 hrs. The mixture was taken up in ether (250 ml), washed with aqueous $NaHCO_3$ (2 x 10 ml), dried, and the solvent removed. Fractional distillation afforded ethylidene diacetate (55) (1.5 ml), b.p. 166 - 168° (Lit. cit.[88] b.p. 166 - 168°), ν_{max} 1768, 1208, 1078 cm^{-1}, P.m.r. δ1.42 (doublet J = 5 Hz (CH_3)), 1.98 (OAc), 6.75 (quartet J = 5 Hz, J' = 9 Hz C(1)H (M^+ 146, $C_6H_{10}O_4$ requires 146).

4a,5-Epoxy-c-8a-methyl-*cis*- and *trans*- decahydronaphth-r-1-yl acetate (25b) and (26c)

m-Chloroperbenzoic acid (1.5 g) was added to a solution of c-8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphth-r-1-yl acetate (24b, 1.5 g) in ether (100 ml) and the solution kept at room temperature for 3 hrs. The solution was washed with aqueous $NaHCO_3$ (4 x 100 ml), dried, and the solvent removed. The residue was adsorbed onto alumina (75 g). Elution with pentane afforded 4a,5-epoxy-c-8a-methyl-*trans*-decahydronaphth-r-1-yl acetate (26c) (740 mg), ν_{max} 1735, 1228, 712 cm^{-1}, P.m.r. δ1.15 (CH_3), 2.02 (OAc), 2.92 ($W_{\frac{1}{2}}^{h}$ 6 Hz; C(5)H), 4.79 ($W_{\frac{1}{2}}^{h}$ 16 Hz; C(1)H).

(M^+ 224. $C_{13}H_{20}O_3$ requires 224). Elution with ether: pentane (1:20) afforded 4a,5-epoxy-c-8a-methyl-*cis*-decahydronaphth-r-1-yl acetate (25b) (520 mg), ν_{max} 1735, 1220, 985 cm^{-1}, P.m.r. δ1.08 (CH_3), 2.03 (OAc) 2.92 ($W_{\frac{1}{2}}^h$ 7 Hz C(5)H), 5.00 ($W_{\frac{1}{2}}^h$ 16 Hz; C(1)H) (M^+ 224. $C_{13}H_{20}O_3$ requires 224).

8a-Methyl-*cis*-decahydronaphthalene-r-1,c-4a-diol (61c)

Lithium aluminium hydride (100 mg) was added to a solution of 4a,5-epoxy-c-8a-methyl-*cis*-decahydronaphth-r-1-yl acetate (25b) (70 mg) in ether (10 ml) and the mixture heated under reflux for 5 hrs. The product was isolated in the usual manner to give 8a-methyl-*cis*-decahydronaphthalene-r-1,c-4a-diol (61c) (50 mg), ν_{max} 3400, 1100, 1040 cm^{-1}, P.m.r. δ1.37 (CH_3), 3.45 (OH), 3.55 (OH), 3.80 ($W_{\frac{1}{2}}^h$ 8 Hz; C(1)M) (M^+ 184, $C_{11}H_{20}O_2$ requires 184).

c-4a-Hydroxy-8a-methyl-*cis*-decahydronaphth-r-1-yl acetate (61a)

A solution of 8a-methyl-*cis*-decahydronaphthalene-r-1,c-4a-diol (61c) (50 mg) in pyridine (5 ml) and acetic anhydride (0.8 ml) was kept at room temperature for 16 hrs. The solution was taken up in ether (20 ml), washed with 2% H_2SO_4 (10 x 10 ml), dried, the solvent removed, and the residue purified by preparative g.l.c. to give c-4a-hydroxy-8a-methyl-*cis*-decahydronaphth-r-1-yl acetate (61a) (30 mg), ν_{max} 3600, 1740 cm^{-1}, P.m.r.

δ1.03 (CH_3), 2.08 (OAc), 5.03 ($W_{\frac{1}{2}}^{h}$ 16 Hz C(1)H) (M^+ 226. $C_{13}H_{22}O$ requires 226).

8a-Methyl-*trans*-decahydronaphthalene-r-1,t-4a-diol (60a)

Lithium aluminium hydride (100 mg) was added to a solution of 4a,5-epoxy-c-8a-methyl-*trans*-decahydronaphth-r-1-yl acetate (26c) (100 mg) in ether (10 ml) and the mixture heated under reflux for 5 hrs. The product was isolated in the usual manner to give 8a-methyl-*trans*-decahydronaphthalene-r-1,t-4a-diol (60a) (80 mg), ν_{max} 3425 cm^{-1}, P.m.r. δ0.92 (CH_3), 2.43 (OH), 3.75 ($W_{\frac{1}{2}}^{h}$ 15 Hz C(1)H) (M^+ 184, $C_{11}H_{20}O_2$ requires 184).

t-4a-Hydroxy-8a-methyl-*trans*-decahydronaphth-r-1-yl acetate (60b)

A solution of 8a-methyl-*trans*-decahydronaphthalene-r-1,t-4a-diol (60a) (80 mg) in pyridine (5 ml) and acetic anhydride (0.8 ml) was kept at room temperature for 16 hrs. The solution was taken up in ether (20 ml) washed with 2% H_2SO_4 (10 x 10 ml), dried, the solvent removed, and the residue purified by preperative g.l.c. to give t-4a-hydroxy-8a-methyl-*trans*-decahydronaphth-r-1-yl acetate (60b) (42 mg), ν_{max} 3650, 1740, 1235 cm^{-1}, P.m.r. δ1.02 (CH_3), 2.00 (OAc), 5.10 ($W_{\frac{1}{2}}^{h}$ 9 Hz; C(1)H) (M^+ 226. $C_{13}H_{22}O$ requires 226).

BF_3-etherate rearrangement of;

(a) 4a,5-epoxy-c-8a-methyl-*cis*-decahydronaphth-r-1-yl

was added to a solution of 4a,5-epoxy-c-8a-methyl-*cis*-decahydronaphth-r-1-yl acetate (25b) (500 mg) in benzene (20 ml) and the solution stirred for 20 min at room temperature. The solution was washed with aqueous $NaHCO_3$ (4 x 20 ml), dried, and the solvent removed. Preperative g.l.c. of the product afforded c-8a-methyl-1,2,3,7,8,8a-hexahydronaphth-r-1-yl acetate (62a) (80 mg), ν_{max} 3040, 1740, 1240 cm^{-1}, P.m.r. δ1.07 (CH_3), 2.07 (OAc) 2.86 (~~triplet~~ J = 9, J' = 7 Hz; C(1)H), 5.68 ($W_{\frac{1}{2}}^{h}$ 49 Hz; C(4), C(5)H and C(6)H), λ_{max} (cyclohexane) 234 nm (ε22,600) (M^+ 206. $C_{13}H_{18}O_2$ requires 206). and c-8a-methyl-5-oxo-*trans*-decahydronaphth-r-1-yl acetate (32b) (75 mg), ν_{max} 1740, 1715, 1240 cm^{-1}, P.m.r. δ0.85 (CH_3), 2.05 (OAc), 4.75 ($W_{\frac{1}{2}}^{h}$ 13 Hz; C(1)H) (M^+ 224, $C_{13}H_{20}O_3$ requires 224). A sample of the reaction product (200 mg) was adsorbed onto a dry column of alumina and the column developed with ether. Segments of the column were removed and after extraction with methylene chloride afforded a mixture of c-8a-methyl-1,2,3,7,8,8a-hexahydronaphth-r-1-yl acetate (62a), c-8a-methyl-5-oxo-*trans*-decahydronaphth-r-1-yl acetate (32b) and c-8a-methyl-5-oxo-*cis*-decahydronaphth-r-1-yl acetate (31b) (80mg), and a sample of 4a-fluoro-c-5-hydroxy-c-8a-methyl-*trans*-decahydronaphth-r-1-yl acetate (60c) (72 mg), ν_{max} 3525, 1740, 1235, 790 cm^{-1}, P.m.r. δ1.24 (doublet, J = 1.5 Hz (CH_3)), 2.02 (OAc), 3.40 ($W_{\frac{1}{2}}^{h}$ 13 Hz; C(5)H), 4.72 ($W_{\frac{1}{2}}^{h}$ 28 Hz; C(1)H) (M^+ 244. $C_{13}H_{21}O_3F$ requires 244).

(b) 4a,5-epoxy-c-8a-methyl-*cis*-decahydronaphth-r-1-yl acetate (25b). BF_3-etherate (0.3 ml) was added to a solution of 4a,5-epoxy-c-8a-methyl-*cis*-decahydronaphth-r-1-yl acetate (25b) (50) in ether (2.5 ml). After 5 min the reaction was quenched by the addition of aqueous $NaHCO_3$ (5 ml), the ether layer separated, dried, and the solvent removed. The product was adsorbed onto alumina (5 g). Elution with pentane afforded c-8a-methyl-1,2,3,7,8,8a-hexahydronaphth-r-1-yl acetate (62a) (12.5 mg), ν_{max} 3040, 1740, 1240 cm^{-1}, P.m.r. δ1.07 (CH_3), 2.07 (OAc) 2.86 (triplet J = 9, J' = 7 Hz; C(1)H), 5.68 ($W_{\frac{1}{2}}^{h}$ 49 Hz; C(4)H, C(5)H and C(6)H (M^+206. $C_{13}H_{18}O_2$ requires 206). Elution with ether afforded 4a-fluoro-c-5-hydroxy-c-8a-methyl-*trans*-decahydronaphth-r-1-yl acetate (60c)(30 mg), ν_{max}3525, 1740, 1235, 790 cm^{-1}, P.m.r. δ1.24 (doublet, J = 1.5 Hz (CH_3)), 2.02 (OAc), 3.40 ($W_{\frac{1}{2}}^{h}$ 13 Hz; C(5)H, 4.72 ($W_{\frac{1}{2}}^{h}$ 28 Hz; C(1)H) (M^+ 244. $C_{13}H_{21}O_3F$ requires 244).

(c) 4a,5-epoxy-c-8a-methyl-*cis*-decahydronaphth-r-1-yl acetate (25b). To a solution of 4a,5-epoxy-c-8a-methyl-*cis*-decahydronaphth-r-1-yl acetate (25b) (20 mg) in dioxan (1 ml) was added BF_3-etherate (0.1 ml). After 35 mins the reaction was quenched with aqueous $NaHCO_3$. The product was shown to be a mixture (43:18:8) of c-8a-methyl-1,2,3,7,8,8a-hexahydronaphth-r-1-yl acetate (62a), 4a-fluoro-c-5-hydroxy-c-8a-methyl-*trans*-decahydronaphth-r-1-yl acetate (60c) and c-8a-methyl-5-

oxo-*trans*-decahydronaphth-r-1-yl acetate (32b) by co-injection with authentic samples into analytical g.l.c. columns packed with SE 30, carbowax 20M, QF 1, and FFAP on varaport 30.

(d) 4a,5-epoxy-c-8a-methyl-*trans*-decahydronaphth-r-1-yl acetate (26c). BF_3-etherate (0.3 ml) was added to a solution of 4a,5-epoxy-c-8a-methyl-*trans*-decahydronaphth-r-1-yl acetate (26c) in benzene (30 ml) and the solution kept at room temperature for 5 mins. The product was isolated in the usual manner. Preperative g.l.c. on the product mixture gave c-8a-methyl-1,2,3,7,8,8a-hexahydronaphth-r-1-yl acetate (62a) (90 mg), the ring contracted compound (65) (14 mg), ν_{max} 2950, 2780, 1740, 1730 cm^{-1}, P.m.r. δ1.07 (CH_3), 2.02 (OAc), 4.87 ($W_{\frac{1}{2}}^{h}$ 11 Hz C(1)H) 9.4 ($W_{\frac{1}{2}}^{h}$ 3Hz CHO) (M^+224, $C_{13}H_{20}O_3$ requires 224); c-8a-methyl-5-oxo-*cis*-decahydronaphth-r-1-yl acetate (31b)(15 mg), ν_{max} 1740, 1730, 1240 cm^{-1}, P.m.r. δ1.10 (CH_3), 2.03 (OAc), 4.83 ($W_{\frac{1}{2}}^{h}$ 14 Hz, C(1)H) (M^+224, $C_{13}H_{20}O_3$ requires 224); c-8a-methyl-5-oxo-*trans*-decahydronaphth-r-1-yl acetate (32b) (7 mg), ν_{max} 1740, 1715, 1240 cm^{-1}, P.m.r. δ0.85 (CH_3), 2.05 (OAc), 4.75 ($W_{\frac{1}{2}}^{h}$ 29 Hz, C(1)H) (M^+224, $C_{13}H_{20}O_3$ requires 224); an unidentified ketone (17 mg) ν_{max} 1740, 1720 cm^{-1}, P.m.r. δ0.95, 2.05, 4.55 ($W_{\frac{1}{2}}^{h}$ 20 Hz), (M^+224); 4a-fluoro-t-5-hydroxy-c-8a-methyl-*cis*-decahydronaphth-r-1-yl acetate (61b)(12 mg), ν_{max} 1740, 1230, 650 cm^{-1}, P.m.r. δ1.01 (doublet J = 4 Hz (CH_3), 2.00 (OAc), 3.65 ($W_{\frac{1}{2}}^{h}$ 10 Hz, C(5)H), 4.73 ($W_{\frac{1}{2}}^{h}$ 22 Hz C(1)H)

(M^+244, $C_{13}H_{21}O_3F$ requires 244); and an unidentified compound (13 mg), ν_{max} 1735, 1670 cm^{-1}, P.m.r. δ1.27, 2.08, 4.35 ($W\frac{h}{2}$ 18 Hz), 5.83 ($W\frac{h}{2}$ 3 Hz) (M^+ 224).

c-8a-Methyl-1,2,3,7,8,8a-hexahydronaphthalen-r-1-ol (62b)

L.A.H. (0.1g) was added to a solution of c-8a-methyl-1,2,3,7,8,8a-hexahydronaphth-r-1-yl acetate (62a) (70 mg) in ether (5 ml) and the mixture kept at room temperature for two hours. Isolation of the product in the usual manner gave c-8a-methyl-1,2,3,7,8,8a-hexahydronaphthalen-r-1-ol (62b) (50 mg), ν_{max} 3400 cm^{-1}, P.m.r. δ0.99 (CH_3) 3.53 (triplet J, J' = 7 Hz C(1)H), 5.65 ($W\frac{h}{2}$ 30 Hz C(4)H, C(5)H and C(6)H (M^+ 164. $C_{11}H_{16}O$ requires 164).

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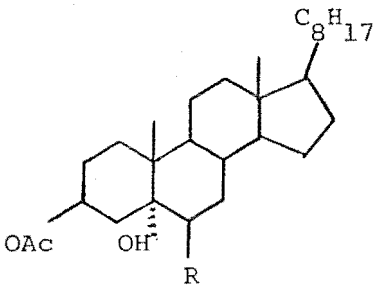

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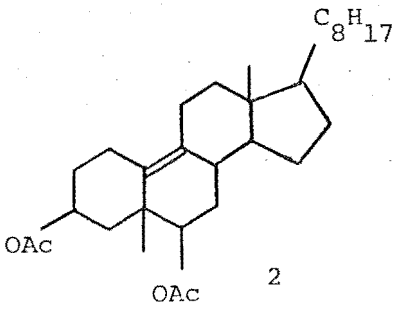
1b R = CH_3



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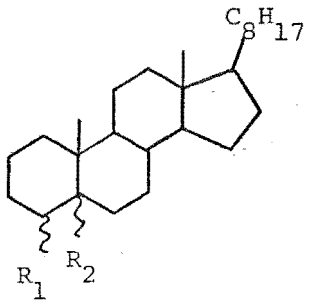


3a R_1 = βOAc, R_2 = αOH

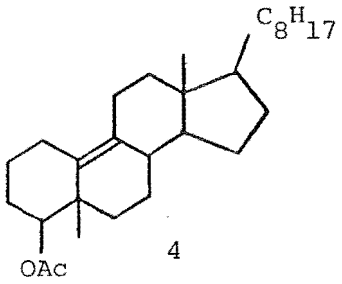
3b R_1 = αOAc, R_2 = αOH

3c R_1 = βOAc, R_2 = βOH

3d R_1 = βOAc, R_2 = βOAc

3e R_1 = H , R_2 = αOH

3f R_1 = αD , R_2 = αOH



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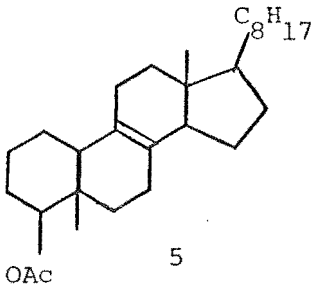

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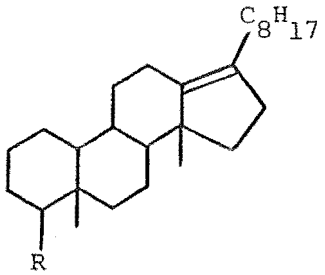

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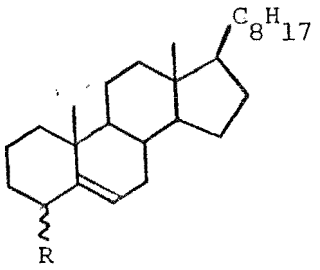
6b R = H



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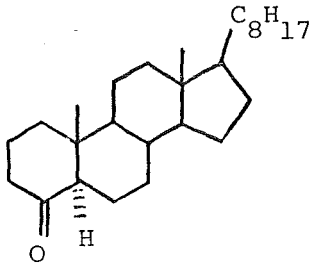
7b R = βOAc

7c R = H

7d R = αD



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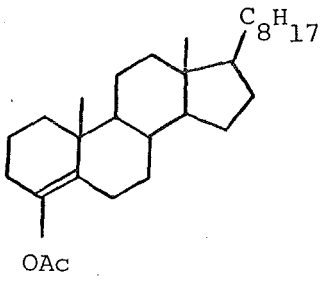

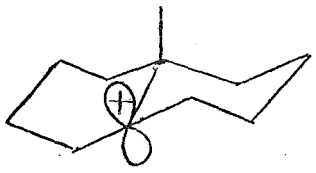

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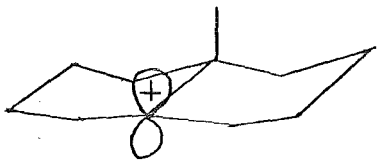

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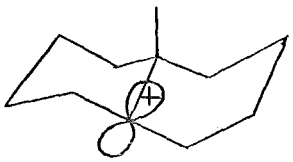

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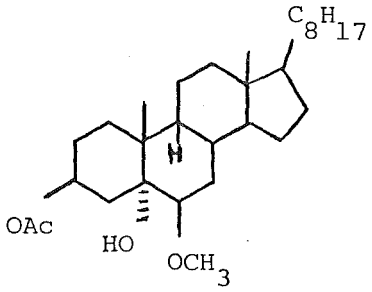

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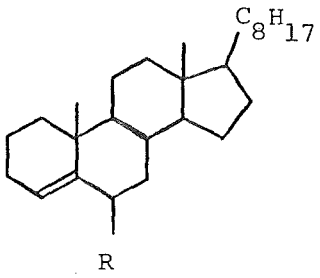
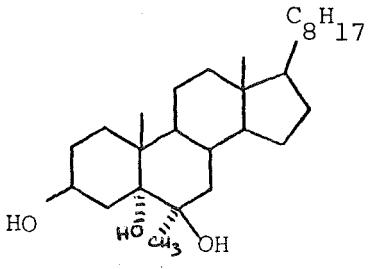


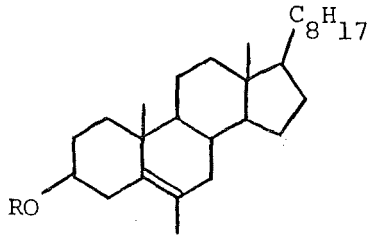
14a R = H

14b R = αOAc

14c R = βOAc

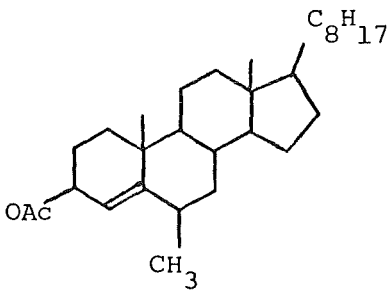


15

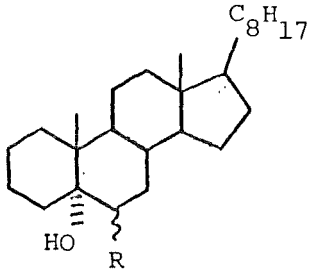


16a R = H

16b R = Ac

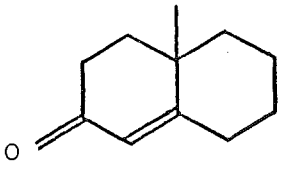


17

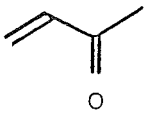


18a R = αOAc

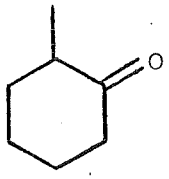
18b R = βOAc



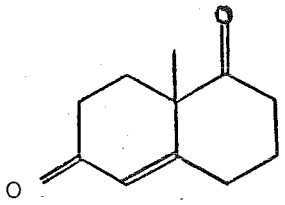
19



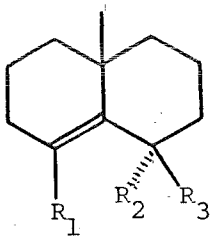
20



21



22



23a R_1 = H, R_2 = R_3 = H

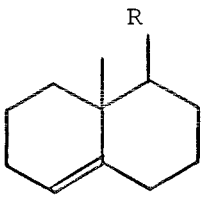
23b R_1 = D, R_2 = R_3 = H

23c R_1 = R_2 = H, R_3 = D

23d R_1 = R_3 = H, R_2 = D

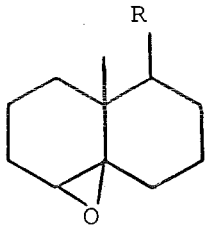
23e R_1 = OAc, R_2 = R_3 = H

23f R_1 = R_2 = H, R_3 = OAc



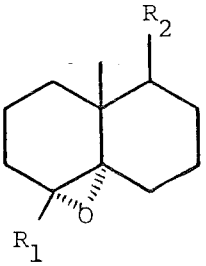
24a R = OH

24b R = OAc



25a R = OH

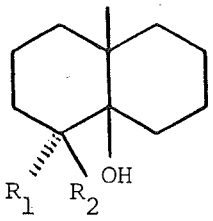
25b R = OAc



26a R_1 = R_2 = H

26b R_1 = D, R_2 = H

26c R_1 = H, R_2 = OAc

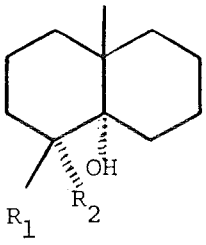


27a R_1 = R_2 = H

27b R_1 = D, R_2 = H

27c R_1 = OH, R_2 = H

27d R_1 = H, R_2 = OH



28a R_1 = R_2 = H

28b R_1 = D, R_2 = H

28c R_1 = OH, R_2 = H

28d R_1, R_2 = O

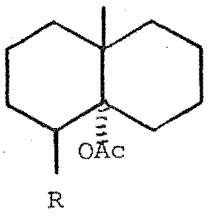
28e R_1 = OH, R_2 = D

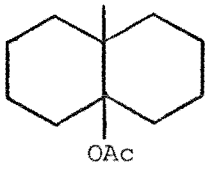
28f R_1=OMs, R_2 = D

28g R_1 = H, R_2 = D

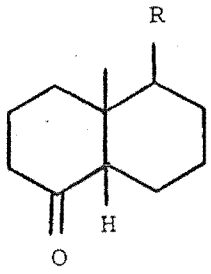
28h R_1 = OAc, R_2 = H

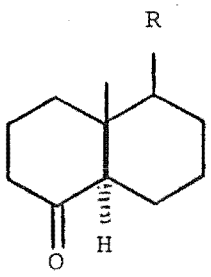
28i R_1 = H, R_2 = OH





30





29a R = H

29b R = OAc

31a R = H

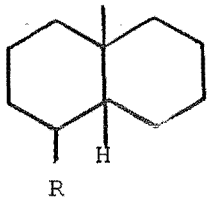
31b R = OAc

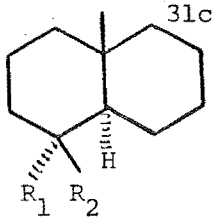
31c R = OH

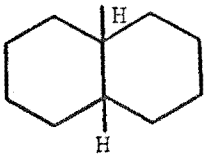
32a R = H

32b R = OAc

32c R = OH







35

33a R = OAc

33b R = OH

33c R = H

34a R_1 = OAc, R_2 = H

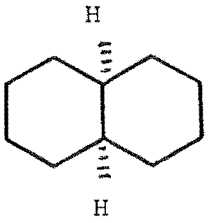
34b R_1 = R_2 = H

34c R_1 = OH, R_2 = H

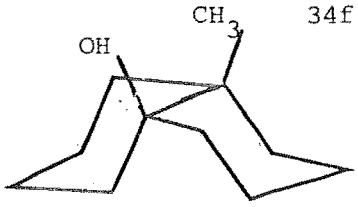
34d R_1 = H, R_2 = OH

34e R_1 = OAc, R_2 = OH

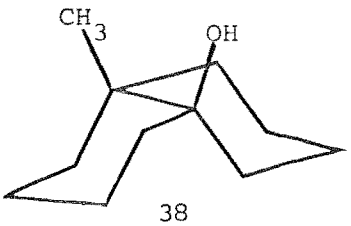
34f R_1 = H, R_2 = OAc



36



37



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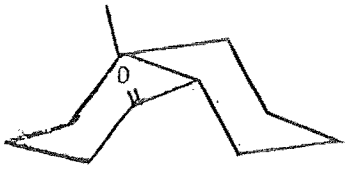

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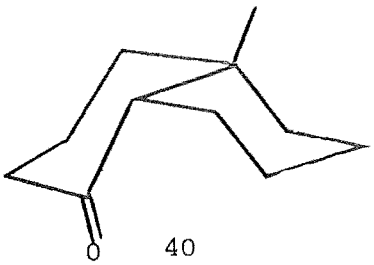

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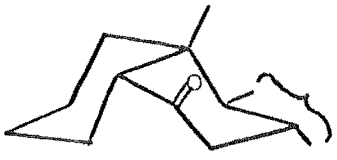

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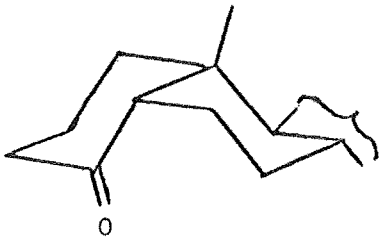

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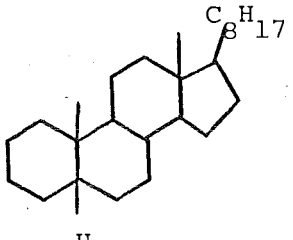
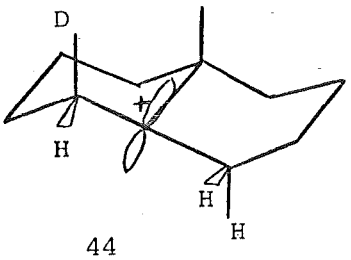


43



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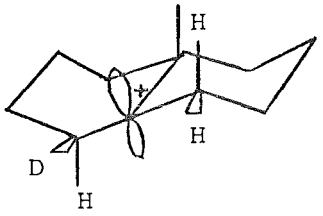
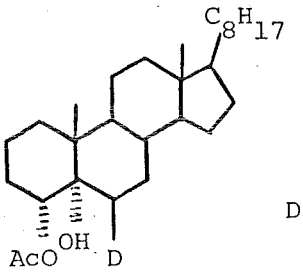
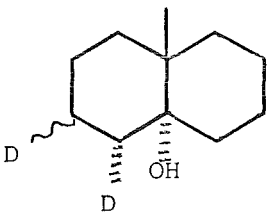


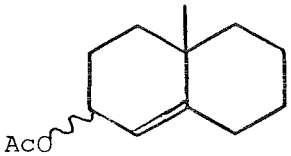
45



46



47



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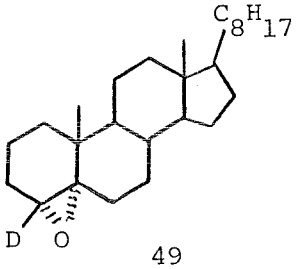
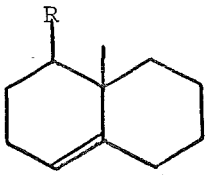
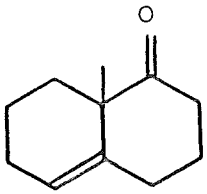
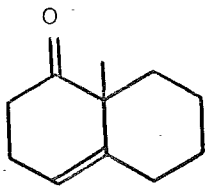


49





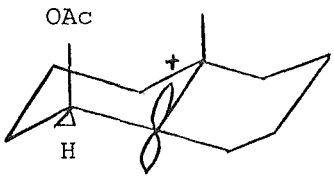
51



52

50a R = OAc

50b R = OH



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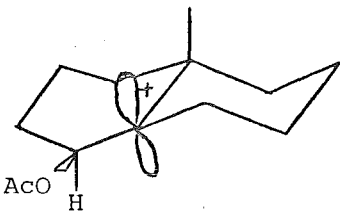

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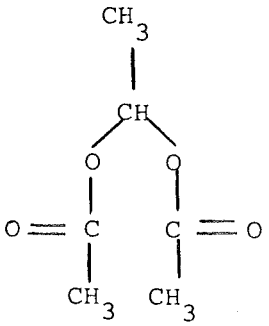

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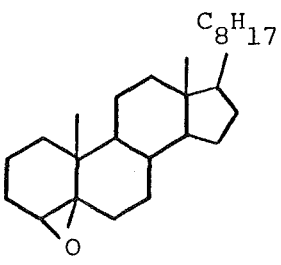

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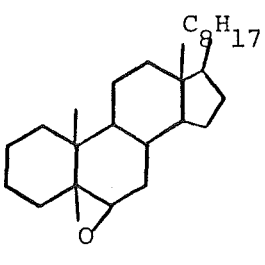

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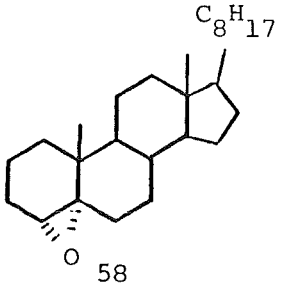

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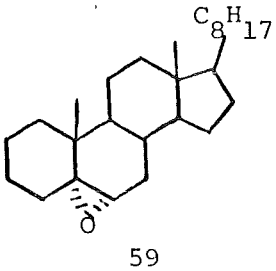
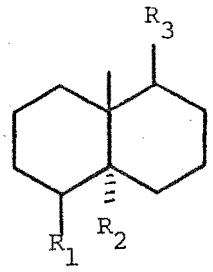


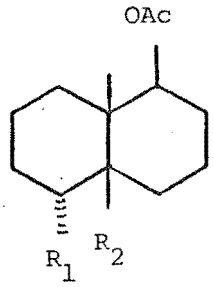
59



60a $R_1 = R_3 = OH$, $R_2 = H$

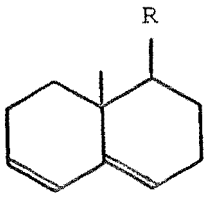
60b $R_1 = OH$, $R_2 = H$, $R_3 = OAc$

60c $R_1 = OH$, $R_2 = F$, $R_3 = OAc$



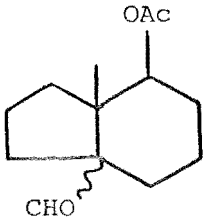
61a $R_1 = OH$, $R_2 = H$,

61b $R_1 = OH$, $R_2 = F$,

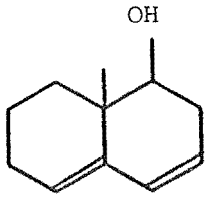


62a R = OAc

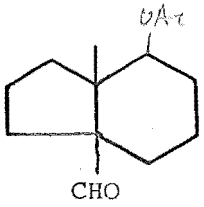
62b R = OH



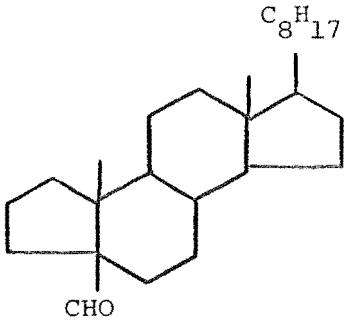
63



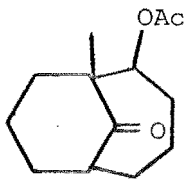
64



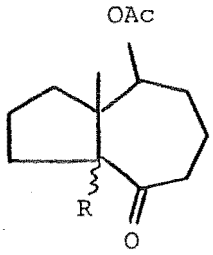
65



66

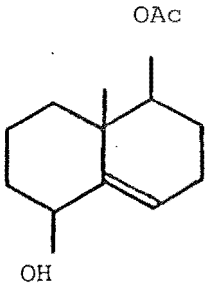


67

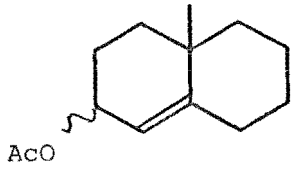


68a R = αH

68b R = βH



69



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